



# Impact of COVID-19 on Anemia, Polypharmacy and Medication Use: A Retrospective Analysis of Pre- and Post-infection Health Outcomes

COVID-19'un Anemi, Polifarmasi ve İlaç Kullanımı Üzerindeki Etkisi: Enfeksiyon Öncesi ve Sonrası Sağlık Sonuçlarının Retrospektif Analizi

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## ABSTRACT

**Aim:** This study aimed to investigate the impact of coronavirus disease 2019 (COVID-19) infection on anemia, polypharmacy, inappropriate medication use, and the prescription of antidepressants, antipsychotics, and analgesics. Specifically, it compared medication use and associated health outcomes before and after COVID-19 infection.

**Materials and Methods:** A retrospective analysis was conducted using data from the national health registry system, including 354 patients who had COVID-19 between March 2020 and December 2022. Data on comorbidities, medication use, and hemoglobin levels were collected for six months before and after COVID-19 diagnosis.

**Results:** The study revealed significant increases in anemia, polypharmacy, antidepressant use, antipsychotic use, and analgesic use post-COVID-19 infection ( $p<0.05$ ). Subgroup analyses showed significant increases in analgesic use, including paracetamol, non-steroidal anti-inflammatory drugs, opioids, and gabapentinoids (gabapentin and pregabalin). Multivariate logistic regression indicated that antipsychotic use after COVID-19 infection independently increased the likelihood of anemia (odds ratio: 2.99, 95% confidence interval: 1.08-8.29,  $p<0.05$ ).

**Conclusion:** The study found significant increases in anemia, polypharmacy, and the use of antidepressants, antipsychotics, and analgesics following COVID-19 infection. These findings emphasize the need for careful monitoring of medication use and anemia in post-COVID-19 patients and highlight the importance of appropriate prescription practices to mitigate long-term healthcare risks.

**Keywords:** Anemia, polypharmacy, antidepressants, COVID-19 pandemic

## ÖZ

**Amaç:** Bu çalışma, 2019 koronavirüs hastalığı (COVID-19) enfeksiyonunun anemi, polifarmasi (çoklu ilaç kullanımı), uygunsuz ilaç kullanımı ve antidepressan, antipsikotik ile analjezik reçetelenmesi üzerindeki etkilerini araştırmayı amaçlamıştır. Özellikle, COVID-19 enfeksiyonu öncesi ve sonrası dönemdeki ilaç kullanımı ve ilişkili sağlık sonuçları karşılaştırılmıştır.

**Gereç ve Yöntem:** Mart 2020 ile Aralık 2022 tarihleri arasında COVID-19 geçirmiş 354 hastayı içeren ulusal sağlık kayıt sistemi verileri kullanılarak retrospektif bir analiz gerçekleştirilmiştir. COVID-19 tanısından önceki ve sonraki altı aylık dönemler için hastaların ek hastalıkları, ilaç kullanımları ve hemoglobin düzeyleri toplanmıştır.

**Bulgular:** Çalışmada, COVID-19 sonrası dönemde anemi, polifarmasi, antidepressan, antipsikotik ve analjezik kullanımında anlamlı artışlar tespit edilmiştir ( $p<0,05$ ). Alt grup analizlerinde; parasetamol, nonsteroid antiinflamatuar ilaçlar, opioidler ve gabapentinoidler (gabapentin ve pregabalin) dahil olmak üzere analjezik kullanımında da anlamlı artışlar görülmüştür. Çok değişkenli lojistik regresyon analizine göre, COVID-19

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**Received:** 09.09.2025 **Accepted:** 19.12.2025 **Publication Date:** 04.03.2026

**Cite this article as:** Akbaş ES, Öztürk E, Öztürk ZA. Impact of COVID-19 on anemia, polypharmacy and medication use: a retrospective analysis of pre- and post-infection health outcomes. Nam Kem Med J. 2026;14(1):44-51



sonrası antipsikotik kullanımı, bağımsız olarak anemi riskini artıran bir faktör olarak bulunmuştur (olasılık oranı: 2,99, %95, güven aralığı: 1,08-8,29,  $p<0,05$ ).

**Sonuç:** Bu çalışma, COVID-19 enfeksiyonu sonrası dönemde anemi, polifarmasi ve antidepresan, antipsikotik ile analjezik kullanımında anlamlı artışlar olduğunu ortaya koymuştur. Bu bulgular, COVID-19 sonrası hastalarda ilaç kullanımının ve aneminin dikkatle izlenmesi gerektiğini vurgulamakta ve uzun vadeli sağlık risklerini azaltmak için uygun reçeteleme uygulamalarının önemine dikkat çekmektedir.

**Anahtar Kelimeler:** Anemi, polifarmasi, antidepresanlar, COVID-19 pandemisi

## INTRODUCTION

The novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused one of the largest public health crises worldwide to date. Although the effects of the pandemic are considered to have passed, the economic burden caused by the disease is still impacting governments. After the coronavirus disease 2019 (COVID-19) infection, particularly the increased consumption of certain drug groups has led to an increase in inappropriate drug use. This has led to the development of the Turkish Inappropriate Medication Use in the Elderly (TIME) guideline, which aims to help healthcare professionals write optimal prescriptions and reduce inappropriate medication use in older adults<sup>1</sup>.

Antidepressants are commonly used not only for depression but also for medical conditions such as post-traumatic stress disorder, panic disorder, and obsessive-compulsive disorder. Additionally, they are used for conditions like chronic pain and insomnia<sup>2</sup>. After the COVID-19 infection, it can be said that the use of antidepressants may increase due to the rising issues and economic problems for governments.

So far, the results of case series published on anemia in COVID-19 are generally contradictory. In some, it was reported that the hemoglobin (HGB) concentrations of patients who survived and those who died due to SARS-CoV-2 infection were similar, while no significant difference was found between patients followed in the intensive care unit (ICU) and those outside the ICU. Other studies, however, have reported lower HGB levels in patients with severe disease<sup>3</sup>.

When more than five medications are taken in a day, this is called polypharmacy. The use of such a number of medications increases the likelihood of drug interactions, some of which can lead to more significant health issues. The portion of the used medications whose adverse effects outweigh their expected benefits is referred to as potentially inappropriate medication (PIM)<sup>4</sup>. In Türkiye, the Turkish Geriatrics Academy has developed the TIME criteria in these indications.

In our study, data from the national health registry system were examined for patients who had experienced a COVID-19 infection, comparing the period before the infection with the period after the infection. The aim was to investigate the relationship between anemia, polypharmacy, inappropriate

medication use, and the usage rates of certain medications such as antidepressants, antipsychotics, and analgesics. We hypothesized that COVID-19 infection may increase the prevalence of anemia, polypharmacy, and the use of certain high-risk medications.

## MATERIALS AND METHODS

### Design and Sample

This retrospective study included 620 patients who were admitted to the University Hospital for different diseases and health problems between March 1, 2020 and December 12, 2022 during the COVID-19 pandemic. Of these 620 patients, data on comorbidities and visits to healthcare facilities were available for analysis for 354 patients. This study included only geriatric patients aged 65 years and older with PCR-confirmed COVID-19. The flow diagram of the patients included in the study is shown in Figure 1.

### Ethical Considerations

All procedures for studies involving human participants were performed in accordance with the 1964 Declaration of Helsinki and its subsequent revisions. The study was approved by the Clinical Research Ethics Committee of Gaziantep University (approval number: 2022/10, date: 07.02.2022).

### Data Collection

Data for all patients, including comorbidities, prescriptions, and the number of medications they should be taking for chronic diseases, were obtained by scanning the national health registry system, where health records are stored for at least 8 years. Anemia was defined according to the World Health Organization (WHO) HGB thresholds, and comorbidities were identified based on documented ICD-10 diagnostic codes within the national health registry system. Anemia was defined as HGB <13 g/dL in men and <12 g/dL in non-pregnant women according to WHO criteria<sup>5</sup>. The study period was divided into two parts: 6 months before and 6 months after the diagnosis of COVID-19 for each patient. COVID-19 diagnosis for each patient was confirmed using the polymerase chain reaction (PCR) method, and the recovery period was determined through subsequent PCR tests. Polypharmacy is defined as the simultaneous use of five or more medications. Polypharmacy was recorded if at least

three prescriptions for five or more medications were regularly prescribed within 4 weeks or less from the date of COVID-19 diagnosis. The patients' inappropriate medication use status was determined using the TIME guideline.

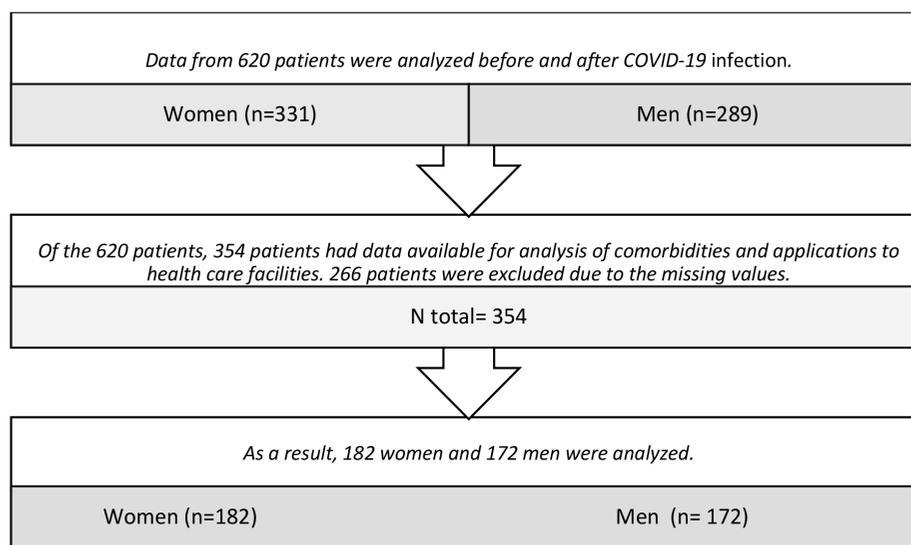
### Statistical Analysis

The statistical analysis of the study was performed using IBM SPSS for Windows 24.0 statistical software. Parametric tests were applied to data showing normal distribution, while non-parametric tests were used for data not showing normal distribution. The normality of the data was evaluated using the Kolmogorov-Smirnov and Shapiro-Wilk normality tests. Descriptive statistical methods, including frequency, mean, standard deviation, median, minimum, and maximum values, were used to compare quantitative data. The significance of the difference between the means of two normally distributed groups was determined by the paired samples t-test, while the Wilcoxon signed-rank test was applied for data not showing normal distribution. McNemar's test was used to evaluate the relationship between categorical variables, and Pearson's correlation coefficient was calculated to assess the relationship between numerical variables. Multivariate binary logistic regression analysis was performed to determine the independent factors related to the parameters. In the multivariate binary logistic regression analysis, all variables listed in Table 4 were included in the model. Sex, age, length of hospital stays, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease, polypharmacy status (before and after COVID-19), total number of medications (before and after COVID-19), antipsychotic use after infection,

and analgesic use before infection were entered as independent variables. Potential confounders, including age, sex, and major chronic comorbidities, were adjusted for in the final model to reduce bias and to ensure the robustness of the estimated associations. Results with a p-value less than 0.05 were considered statistically significant.

### RESULTS

In our retrospective study, 620 geriatric patients with a COVID-19 infection history from the national health system records were included. Due to missing data, 266 participants were excluded, leaving 354 patients (182 women and 172 men) for analysis. A total of 354 geriatric patients (182 women, 172 men) were included in the final analysis (Figure 1). Descriptive data and comparisons of age, days of hospitalization during active COVID-19 infection, medications used for comorbidities, and HGB levels in both genders are shown in Table 1. It was found that men had a longer hospital stay due to COVID-19 infection ( $p < 0.05$ ). In our study, a comparison was made between the six months before and after the diagnosis of COVID-19 regarding anemia, pharmaceutical status, and the prescription of various drugs (Table 2). It was determined that anemia, polypharmacy ( $p < 0.001$ ), antidepressant use ( $p < 0.05$ ), antipsychotic use, and analgesic use significantly increased ( $p < 0.01$ ). In subgroup analyses, it was found that the use of analgesics such as paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and gabapentinoid (GABA) analogues significantly increased ( $p < 0.01$ ). Table 3 summarizes the comparison of polypharmacy, antidepressant and analgesic prescriptions, and anemia in the six months



**Figure 1.** Flow diagram of the patients included in the study

COVID-19: Coronavirus disease 2019

**Table 1. Descriptive data and comparisons of patients' age, days hospitalized during active COVID-19 disease, medications for comorbidities and hemoglobin levels in both sexes**

Variables	Total		Gender (n=354)				p
			Women (n=182)		Men (n=172)		
	Mean (median)	SD (min-max)	Mean (median)	SD (min-max)	Mean (median)	SD (min-max)	
Age <sup>0</sup>	73.06 (72)	(65-96)	73.82 (72)	(65-96)	72.25 (71)	(65-91)	0.021*
Duration of hospital stay <sup>00</sup>	7.9 (7)	(0-37)	7.18 (7)	(0-24)	8.66 (7)	(0-37)	0.037*
Regular drugs before <sup>10</sup>	5.01 (5)	(0-13)	5.03 (5)	(0-13)	4.98 (6)	(0-15)	0.882
Regular drugs after <sup>20</sup>	6.49 (6)	(0-15)	6.48 (5)	(0-13)	6.51 (6)	(0-14)	0.994
HGB before <sup>30</sup>	13.43	±1.64	12.935	±1.42	13.96	±1.69	<0,001*
HGB after <sup>40</sup>	13.02 (13.18)	(8.1-17.3)	12.7 (12.9)	(8.1-16.9)	13.2 (13.6)	(8.1-17.3)	0.006*

<sup>0</sup>Mann-Whitney U test was performed for non-parametric data. Mean values were also given for non-parametric data.

<sup>00</sup>Student's t-test used for parametric data. Mean and standard deviation values were used instead of median and minimum maximum values for parametric data.

\*Significant at 0.05 level.

<sup>0</sup>: Length of the index COVID-19 hospital admission only.

<sup>1</sup>: Number of drugs regularly prescribed to patients for their chronic diseases in the six months before COVID-19.

<sup>2</sup>: Number of drugs regularly prescribed to patients for their chronic diseases in the six months after COVID-19.

<sup>3</sup>: Hemoglobin values of the patients in the six months before COVID-19.

<sup>4</sup>: Hemoglobin values of the patients in the six months after COVID-19.

COVID-19: Coronavirus disease 2019, HGB: Hemoglobin, SD: Standard deviation

before and after the COVID-19 diagnosis, by gender. In the female group, the use of polypharmacy and analgesic subgroups including paracetamol, NSAIDs, opioids, and GABA analogues significantly increased ( $p < 0.05$ ). In the male group, it was found that anemia, polypharmacy, antidepressant use, and analgesic subgroups such as paracetamol, NSAIDs, and opioids increased significantly ( $p < 0.05$ ). The multivariate logistic regression analysis of independent variables for anemia in the six months before and after the COVID-19 diagnosis is shown in Table 4. Accordingly, antipsychotic drug use after COVID-19 infection was found to independently and positively increase the presence of anemia [odds ratio (OR) 2.99, 95% confidence interval (CI): 1.08-8.29,  $p < 0.05$ ].

## DISCUSSION

In our study, we determined that the rates of anemia, polypharmacy, antidepressant use, antipsychotic use, and analgesic use significantly increased in the period following the COVID-19 infection. Additionally, through regression analysis, we found that the use of antipsychotic drugs after COVID-19 infection independently increased the occurrence of anemia in these patients.

The relationship between COVID-19 and anemia is complex. Both anemia and COVID-19 lead to immune system dysfunction, making patients more susceptible to autoimmune complications that can effectively transform into one another<sup>6,7</sup>. Inflammation causes characteristic changes in iron homeostasis. This results in increased iron uptake and accumulation in macrophages, along with a decrease in iron absorption from the intestines<sup>8</sup>. This situation leads to a decrease in circulating iron levels. Additionally, it results in a reduction of the metal levels necessary for erythropoiesis. As a result, anemia of inflammation occurs due to cytokines that inhibit erythropoiesis, shortened erythrocyte lifespan, and decreased biological activity of erythropoietin<sup>9,10</sup>. In our study, anemia increased among male patients following COVID-19 infection, whereas no significant change was observed in females. Only a limited number of studies have evaluated HGB levels in COVID-19 patients by sex. Therefore, our findings regarding the post-infection increase in anemia among male patients provide a novel contribution to the literature. Notably, the increase in anemia was statistically significant only in men.

In a previous study, the identification of anemia as an independent risk factor for the prognosis of COVID-19 patients<sup>11</sup> highlights the importance of the disease's impact on hematological parameters.

**Table 2. Medication use and anemia before and after COVID-19**

Variables	Period				p
	Before COVID-19		After COVID-19		
	n	%	n	%	
<b>Anemia</b>	91	25.7	118	33.3	<b>&lt;0.001*</b>
<b>Polypharmacy</b>	189	53.4	265	74.9	<b>&lt;0.001*</b>
<b>Potentially inappropriate medication use (TIME criteria)</b>	113	31.9	122	34.5	0.396
<b>Antidepressant use</b>	78	22.0	98	27.7	<b>0.021</b>
Escitalopram	36	10.2	46	13.0	0.175
Sertraline	10	2.8	12	3.4	0.791
Duloxetine	16	4.5	22	6.2	0.238
Mirtazapine	6	1.7	10	2.8	0.344
Amitriptyline	5	1.4	9	2.5	0.289
Fluoxetine	4	1.1	1	0.3	0.375
Paroxetine	3	0.8	3	0.8	1.000
Trazodone	3	0.8	6	1.7	1.000
Venlafaxine	2	0.6	3	0.8	1.000
<b>Benzodiazepine use</b>	15	4.2	17	4.8	0.832
Medazepam	11	3.1	14	4.0	0.629
Alprazolam	3	0.8	3	0.8	1.000
<b>Antipsychotic</b>	8	2.3	20	5.6	<b>0.008*</b>
Quetiapine	4	1.1	9	2.5	0.180
Haloperidol	1	0.3	2	0.6	1.000
Olanzapine	1	0.3	4	1.1	0.250
Risperidone	1	0.3	3	0.8	0.625
Aripiprazole	1	0.3	1	0.3	1.000
<b>Analgesic use</b>	327	92.4	336	94.9	<b>0.004*</b>
Paracetamol	255	72.0	290	81.9	<b>&lt;0.001*</b>
NSAIDs	272	76.8	291	82.2	<b>&lt;0.001</b>
Opioid	38	10.7	58	16.4	<b>&lt;0.001*</b>
GABA	43	12.1	65	18.4	<b>&lt;0.001*</b>

\*Significant at 0.05 level, The McNemar test was performed for independent categorical data.

TIME: Turkish Inappropriate Medication Use in the Elderly, NSAIDs: Non-steroidal anti-inflammatory drugs, GABA: Gabapentinoids (gabapentin or pregabalin), COVID-19: Coronavirus disease 2019

In elderly patients, the presence of multiple comorbidities is common, leading to the use of numerous medications. Additionally, the physiological functions of older patients decline, and pharmacodynamic and pharmacokinetic changes increase the risk of drug interactions<sup>12</sup>. Drug-drug interactions can exacerbate these undesirable side effects. Polypharmacy ranks third among the causes of hospitalization in elderly patients and is also the leading cause of hospital-associated diseases<sup>13</sup>.

In a cross-sectional study conducted by Chen et al.<sup>13</sup> on COVID-19 patients hospitalized with a diagnosis of COVID-19, high prevalence rates of polypharmacy (77.67%), PIMs (66.99%), and drug-drug interactions (61.65%) were identified.

Additionally, diuretics, followed by benzodiazepines and benzodiazepine receptor agonist hypnotics, insulin, antipsychotics, and rivaroxaban or dabigatran were found to be the most commonly used PIMs. In our study, we also found that the proportion of polypharmacy patients increased after COVID-19 infection. It is well known that polypharmacy and inappropriate medication use lead to negative health outcomes for patients. In this study, no significant difference was observed in the rates of inappropriate medication use before and after COVID-19 (31.9% and 34.5%, respectively;  $p=0.396$ ). This finding differs from the high PIMs rate (66.9%) reported by Chen et al.<sup>13</sup> This discrepancy may be due to differences in study populations, variations in healthcare

**Table 3. Comparison of polypharmacy, antidepressant and analgesic prescriptions and anemia in both sexes in the six months before and after diagnosis of COVID-19 disease**

Gender	Variables	Period				p
		Before COVID-19		After COVID-19		
		n	%	n	%	
Women	Anemia	43	23.6	48	26.4	0.511
	Polypharmacy	96	52.7	134	73.6	<0.001*
	Antidepressant use	50	27.5	58	31.9	0.256
	Analgesic use	170	93.4	175	96.2	0.063
	Paracetamol	137	75.3	149	81.9	0.017*
	NSAIDs	146	80.2	156	85.7	0.013*
	Opioid	17	9.3	30	16.5	<0.001*
	GABA	26	14.3	43	23.6	<0.001*
Men	Anemia	48	27.9	70	40.7	<0.001*
	Polypharmacy	93	54.1	131	76.2	<0.001*
	Antidepressant use	28	16.3	40	23.3	0.045*
	Analgesic use	157	91.4	161	93.6	0.125
	Paracetamol	118	68.6	141	82.0	<0.001*
	NSAIDs	126	73.3	135	78.5	0.049*
	Opioid	21	12.2	28	16.3	0.016*
	GABA	17	9.9	22	12.8	0.063

\*Significant at 0.05 level

The McNemar test was performed for independent categorical data.

NSAIDs: Non-steroidal anti-inflammatory drugs, GABA: Gabapentinoids (gabapentin or pregabalin), COVID-19: Coronavirus disease 2019

system practices, and the use of different criteria for assessing inappropriate medication use.

Worldwide, significant research is being conducted to assess changes in the rates of psychological disorders and psychiatric diagnoses associated with the COVID-19 pandemic. These studies are being carried out despite the decreasing trend in the number of SARS-CoV-2 infections and COVID-19 cases, driven by concerns about the potential long-term mental health impacts of the pandemic<sup>14,15</sup>. According to national data obtained from the United Kingdom, it has been shown that overall mental health scores have decreased since the start of the pandemic, and the proportion of individuals reporting symptoms of depression has nearly doubled compared to pre-pandemic levels<sup>16</sup>.

Data from Europe and the United States provide reliable evidence showing an increase in antidepressant prescription and pharmacy requests during the pandemic period compared to the pre-pandemic period<sup>16</sup>. In our study, the rates of antidepressant use before and after the COVID-19 period were compared, and in line with the literature, it was determined that the usage increased in the post-pandemic period.

Under the shadow of the COVID-19 pandemic, a second crisis has emerged, resulting in a significant increase in psychiatric

disorders. Along with this rise, the usage rates of antipsychotic medications have inevitably increased<sup>17</sup>.

Long-term use of antipsychotic medications has been clearly associated with an increased risk of death in older adults. Antipsychotics, which cause numerous negative medical effects, have been reported to lead to serious respiratory side effects and are also linked to potential immune function disorders<sup>18</sup>.

A large study conducted with adults from different age groups demonstrated a bidirectional interaction between psychiatric problems and COVID-19. The study found that survivors of COVID-19 are at an increased risk of psychiatric issues, including dementia<sup>18</sup>. Along with this information, it is of great importance to assess the survivors of COVID-19 for depression and psychiatric conditions in the long term and to ensure regular follow-up evaluations.

Hematologic side effects related to psychotropic drugs are very rare, but it should not be forgotten that they can be life-threatening. The hematologic side effects caused by psychotropic drugs have been explained through different pathophysiological mechanisms. These include bone marrow suppression, destruction of immune-related cells, the formation of active or toxic metabolites, and direct bone toxicity<sup>19,20</sup>. In this context, our study provides a noteworthy

**Table 4. Multivariate binary logistic regression analysis of the independent variables for anemia, both prior to and following a six-month period subsequent to a diagnosis of COVID-19**

Variables	B	SE	OR (95% CI)	p-value
Sex	0.714	0.264	2.04 (1.22-3.42)	<b>0.007*</b>
Age	0.057	0.020	1.06 (1.02-1.10)	<b>0.005*</b>
Hospital stay <sup>1</sup>	0.040	0.019	1.04 (1.003-1.080)	0.033
DM <sup>2</sup>	0.379	0.298	1.46 (0.81-2.62)	0.204
CKD <sup>3</sup>	1.980	0.613	7.24 (2.18-24.08)	<b>0.001*</b>
COPD <sup>4</sup>	0.473	0.330	1.61 (0.84-3.07)	0.152
Polypharmacy, before <sup>5</sup>	0.702	0.445	2.02 (0.84-4.83)	0.114
Drugs, before <sup>6</sup>	-0.121	0.128	0.89 (0.69-1.14)	0.343
Polypharmacy, after <sup>7</sup>	-0.474	0.486	0.62 (0.24-1.61)	0.329
Drugs, after <sup>8</sup>	0.212	0.117	1.24 (0.98-1.56)	0.069
Antipsychotics, after <sup>9</sup>	1.098	0.519	2.99 (1.08-8.29)	<b>0.035*</b>
Analgesics, before <sup>10</sup>	-0.553	0.481	0.58 (0.22-1.48)	0.250

\*p<0.05 according to multivariate binary logistic regression analysis. B: Beta, CI: Confidence interval, OR: Odds ratio, COVID-19: Coronavirus disease 2019, SE: Standard error, CKD: Chronic kidney disease, COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, Constant p value =0.22

<sup>1</sup>Length of the index COVID-19 hospital admission only.

<sup>2</sup>Diabetes mellitus

<sup>3</sup>Chronic kidney disease

<sup>4</sup>Chronic obstructive pulmonary disease

<sup>5</sup>Polypharmacy status of the patients before the COVID-19 diagnosis within the last 6 months.

<sup>6</sup>Number of drugs regularly prescribed to patients for their chronic diseases in the six months before COVID-19.

<sup>7</sup>Polypharmacy status of the patients after the COVID-19 diagnosis within the first 6 months.

<sup>8</sup>Number of drugs regularly prescribed to patients for their chronic diseases in the six months after COVID-19.

<sup>9</sup>The number of prescriptions for antipsychotic drugs given to patients within the first six months after their diagnosis of the COVID-19 disease.

<sup>10</sup>The number of prescriptions for analgesic drugs given to patients within the last six months before their diagnosis of the COVID-19 disease

contribution to the literature by demonstrating that post-COVID-19 antipsychotic use is independently associated with anemia, even after adjusting for age, sex, and major comorbid conditions. This independent association suggests that the hematologic vulnerability observed in some patients after COVID-19 infection may be exacerbated by antipsychotic exposure, possibly through one or more of the mechanisms described above. Highlighting the need for closer monitoring of hematologic parameters in patients who require antipsychotic treatment following COVID-19 infection.

One of the known but rare side effects in patients undergoing antipsychotic treatment is anemia. This condition is defined as a decrease in the total number of erythrocytes or the HGB content in red blood cells. The presence of anemia is associated with a reduced capacity of cells to carry oxygen<sup>21,22</sup>. In our study, we found a significant increase in the rate of anemia in patients following a COVID-19 infection. According to the multivariate binary logistic regression analysis results of independent variables related to anemia in the six-month periods before and after the COVID-19 diagnosis, we determined that antipsychotic use after COVID-19 infection independently and positively affected anemia (OR: 2.99, 95% confidence interval

CI: 1.08-8.29, p<0.05). We believe this finding contributes to the literature due to the limited number of studies on this topic.

### Study Limitations

Although our study is a unique one investigating how the frequency of certain conditions changed before and after the COVID-19 diagnosis in patients, it has some limitations. The retrospective nature of the study does not allow for the determination of causal relationships between the results. The data were obtained from a health record system that does not provide precise information about the patient's health status and medication use. It is unknown whether the patient received the treatment in real life, for how long, or the underlying primary cause of the diagnosis recorded in the system. Additionally, the sample size of the study is relatively small. Especially considering the global scale of the pandemic, a larger sample size would have yielded more accurate results.

### CONCLUSION

After COVID-19 infection, we found an increase in the rates of anemia, polypharmacy, antidepressant use, antipsychotic use, and analgesic use in patients. Overall, our study demonstrates

that COVID-19 infection may increase the prevalence of anemia and that antipsychotic use after infection is independently associated with this hematologic complication. Given the limited evidence on this topic, our findings provide important clinical insight and emphasize the need for further prospective studies to confirm the mechanisms and guide safer prescribing practices for post-COVID-19 patients.

## Ethics

**Ethics Committee Approval:** The study was approved by the Clinical Research Ethics Committee of Gaziantep University (approval number: 2022/10, date: 07.02.2022).

**Informed Consent:** This is retrospective study.

## Fotnootes

### Authorship Contributions

Concept: E.S.A., E.Ö., Z.A.Ö., Design: E.S.A., E.Ö., Z.A.Ö., Data Collection or Processing: E.S.A., E.Ö., Z.A.Ö., Analysis or Interpretation: E.S.A., E.Ö., Z.A.Ö., Literature Search: E.S.A., E.Ö., Z.A.Ö., Writing: E.S.A., E.Ö., Z.A.Ö.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

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