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Analysis of the psychiatric consultations requested for hospitalized COVID-19 patients: One year results from a major pandemic hospital

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Ethics Committee Approval
Ethical approval of the study was obtained from the Ethics Committee of Marmara University Medical School (protocol no:092021590)
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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Abstract

Background/Aim: Coronavirus 2019 (COVID-19) has brought unprecedented challenges to the practice of consultation-liaison psychiatry. Moreover, it is probable that the characteristics of psychiatric consultations and administered treatments have varied and will continue to vary significantly over time. Given the relative lack of prior research concerning this issue, this study aimed to provide a multi-dimensional analysis of the psychiatric consultations requested for inpatients diagnosed with COVID-19 and to examine the temporal course of the selected variables throughout the pandemic.

Methods: In this retrospective cohort study, the medical records of 232 patients who underwent psychiatric consultation between May 1, 2020 and April 30, 2021 were reviewed in detail. Data were obtained for a series of variables, including reasons for consultation, diagnoses after assessment, medical comorbidities, past psychiatric history, treatment arrangements, and clinical outcomes, after which the data were systematically classified to be included in the multi-dimensional analysis.

Results: The mean age of the patients was 66.79 (17.18) years (61.21% were males). The most common reasons for consultation were psychomotor agitation, anxiety, and treatment non-compliance, while adjustment disorder and delirium were the most common diagnoses after psychiatric evaluation. Among the reasons for consultation, the shortest durations from admission to consultation were associated with psychomotor agitation, assessment for drug interaction, and treatment non-compliance while among the diagnoses, the duration was shortest for dementia, mental retardation, bipolar disorder, and psychosis. The most frequently prescribed medications were antipsychotics, antidepressants, and benzodiazepines. The number of consultations and rates of delirium and death showed a significant increase over the course of the study. Delirium and medical comorbidities were found to be the strongest predictors of death as a clinical outcome.

Conclusion: Knowledge and experience in the field of consultation-liaison psychiatry might contribute to the accurate diagnosis of COVID-19-related neuropsychiatric syndromes in addition to implementation of appropriate treatment interventions.

Keywords: COVID-19, Consultation-liaison psychiatry, Neuropsychiatry, Psychopharmacology, Delirium, Adjustment disorder

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Introduction

The wide range of clinical presentations among patients treated in Coronavirus 2019 (COVID-19) wards or intensive care units (ICUs) has led to the understanding that the disease is much more frequently associated with multisystemic involvement than previously expected [1, 2]. The most frequently reported clinical manifestations associated with COVID-19 are neuropsychiatric symptoms, which are likely to involve heterogeneous and potentially complex pathophysiological processes [3, 4]. The underlying mechanisms might include several parameters: a) common psychological reactions in response to having the disease, hospitalization, social isolation, severe clinical course, and others; b) direct or indirect effects of the virus on central nervous system (CNS) functions; c) direct effects of medications used for the treatment of COVID-19 or interaction with other drugs; and/or d) abrupt cessation of medications used for an underlying neuropsychiatric disease [5–7]. Aside from anxiety and depressive symptoms that are commonly experienced resulting from psychological stress due to the disease, the most common neuropsychiatric manifestations in the acute period are reported to be delirium/encephalopathy, psychosis, mood changes, and insomnia [8].

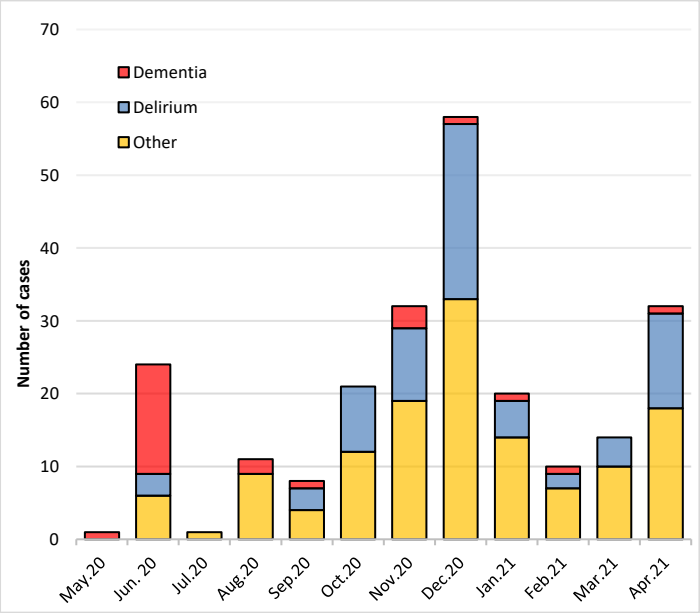
As in other fields of expertise, COVID-19 has brought uncertainty and clinical struggles in the practice of consultation-liaison psychiatry (CLP). The chaotic course of the disease results from multisystemic involvement, frequent updates of treatment protocols, and significant heterogeneity in clinical approaches between hospitals, making it difficult to elucidate the etiology of the neuropsychiatric symptoms in question in addition to developing reliable treatment algorithms [9]. The only known study to date on the characteristics of psychiatric consultations for Turkish patients with COVID-19 was conducted at the initial phase of the pandemic (n = 89) in which it was reported that the most common reason for psychiatric consultation was psychomotor agitation, whereas the most common psychiatric diagnosis was delirium [10]. However, considering the complex interactions among a number of substantial factors (such as the ever-increasing number of infected individuals, frequent updates in treatment algorithms, initiation of vaccination program across the country as of January 2021, and unpredictable mutations in the virus genome), it seems highly probable that the clinical profile of the inpatients and characteristics of psychiatric consultations in COVID-19 wards might exhibit significant changes over the time course of the study.

Taking the above-mentioned limitations into consideration, the present study aimed to provide a multidimensional picture of the characteristics of psychiatric consultations requested for patients hospitalized with a diagnosis of COVID-19 during the one-year period from the onset of the pandemic in Turkey and to assess the cross-sectional relationships between these features in addition to their temporal pattern throughout the pandemic. The variables of interest include the sociodemographic characteristics of the patients, the main characteristics of the psychiatric consultations (reasons for consultation, diagnoses after psychiatric evaluation, past psychiatric diagnoses, treatment protocols, and others) in addition to the clinical features of the cases (medical comorbidity, length of hospital stay, need for intensive care, clinical outcomes, and others).

Materials and methods

The study sample consisted of adult (>18 years old) inpatients admitted to the pandemic hospital (Marmara University, Prof. Dr. Asaf Ataseven Hospital) with a diagnosis of COVID-19 between May 1 2020 and April 30, 2021 and who underwent psychiatric consultation during their hospital stay (the hospital has been serving as the leading center for the treatment of COVID-19 patients in Istanbul since the onset of the pandemic with around 6000 inpatients treated during the first year of service). Data collection was based on the retrospective screening of the patients' medical records, psychiatric consultation files, and other relevant medical information through the hospital's database. Patients with uncompleted procedures (missing information, unsubmitted consultation, and other parameters) or those with unavailable data on corresponding fields were not included in the final sample. Accordingly, a total of 285 psychiatric consultation records (30 cases with two or more files) over a one-year period were examined in detail, and 232 patients who met the criteria were included in the final sample (the monthly distribution of the consultations is shown in Figure 1).

Figure 1: One-year course of the psychiatric consultations requested for inpatients diagnosed with Coronavirus 2019 (COVID-19) and monthly distribution of the psychiatric diagnoses



For each patient, the medical records regarding a series of variables (reasons for psychiatric consultation, diagnoses after evaluation, and medical comorbidities, among others) were reviewed twice and independently by two researchers to reduce potential bias after which the data were systematically classified under corresponding categories, which were determined in accordance with the frequency and clustering tendencies (such as psychomotor agitation, treatment non-compliance, and others, which were coded as the categories for reasons for consultation; psychotic disorders, dementia, and others were coded as psychiatric diagnoses after evaluation).

To include all the relevant data in the statistical analysis, additional levels were provided for the variables potentially consisting of more than one component (such as up to three

levels for reasons for consultation, and up to two levels for diagnoses after consultation). Ethical approval of the study was obtained from the Ethics Committee of Marmara University Medical School (protocol no: 092021590).

Statistical analysis

SPSS (version 24.0) was used for statistical analysis. Descriptive statistics are given as numbers (n), percentages (%), means and standard deviations (SD), median, minimum and maximum values. Normal distribution was assessed using Kolmogorov–Smirnov and Shapiro–Wilk tests. A chi-square test was used to compare the distribution of categorical variables between two independent groups, a Mann–Whitney U test was used to compare non-normally distributed continuous or ordinal variables, Student's-t test was used to compare normally-distributed continuous variables, and Spearman's correlation test were used for the analysis of bidirectional relations between the variables of interest. Logistic regression was used to determine the factors predicting death as an outcome among the patients who underwent psychiatric consultation. Statistical significance was determined as $\alpha = 0.05$.

Results

Sociodemographic and clinical characteristics of the sample

Ninety (38.79%) of the patients were women. The mean age was 65.92 (18.66) (median = 71) for females, 67.33 (16.22) (median = 70) for males, and 66.79 (17.18) (median = 70) for the entire sample. Over half of the patients (54.7%) did not have any psychiatric diagnosis or treatment history prior to hospitalization. Of the 105 patients with a history of psychiatric diagnosis (86 single, 19 two diagnoses), 47.61% (n = 50) had dementia, 24.76% (n = 26) had anxiety disorder, and 12.38% (n=13) had psychotic disorder. It was found that all patients were diagnosed with dementia, bipolar, and/or psychotic disorders; 93.75% (n = 15) of those diagnosed with depressive disorder and 68.18% (n = 15) of those diagnosed with anxiety disorder also had these diagnoses during the pre-admission period. Seventy-two (31.03%) of the patients were actively using at least one psychotropic medication before hospitalization while 10.77% (n = 25) were using other types of CNS drugs (antidementia, antiepileptic, antiparkinsonian, and others). One-hundred forty-two (61.20%) of the patients of the patients had at least one medical comorbidity. Fifty-one (35.91%) had diabetes mellitus (DM), 18.30% (n = 26) had chronic obstructive pulmonary disease (COPD), and 59.85% (n = 85) had other chronic diseases.

General characteristics of the psychiatric consultations

The reasons for the psychiatric consultations and the characteristics of the diagnoses after psychiatric evaluation are shown in Tables 1 and 2. The consultation requests involved two major reasons in 31.89% (n = 74) of the cases and three major reasons in 3.01% (n = 7). On the other hand, 9.05% (n = 21) of the patients received two diagnoses after the psychiatric evaluation. Psychomotor agitation (25.63%, n = 82), anxiety (15%; n = 48), treatment non-compliance (14.69%; n = 47), insomnia (14.06%; n = 45), and confusion (10%; n = 32) were the most common reasons for consultation requested by the treating physicians. The most common reason for consultation was psychomotor agitation in men (29.76%; n = 61) and anxiety in women (19.13%; n = 22). The mean duration from admission to the first consultation was 7.19 (7.77) days (median = 5). In terms of the reasons for consultation, the shortest durations were associated with a request for the evaluation for drug–drug interactions with 2.07 (0.26) days (median = 2), treatment non-compliance with 5 (2.32) days (median = 5), and psychomotor agitation with 5.89 (6.13) days (median = 4). The most common diagnoses established by the consultant psychiatrists were adjustment disorder (AD) (29.25%; n = 74) and delirium (28.85%; n = 73) for the whole sample; delirium was the most common diagnosis among males (32.45%; n = 49) and AD among females (30.39%; n = 31). Among the primary diagnoses, the mean age was highest for dementia (79.58 (8.23) years) and delirium (76.41 (11.99) years) and lowest for bipolar disorder (44.50 (21.92) years) and alcohol/substance use disorder ([ASUD], 31 (1.41) years) as shown in Table 2. Finally, the highest rates of medical comorbidity were observed among patients diagnosed with AD with depressed mood (AD-D) at 76.47%, delirium (75.34%), and depressive disorder (62.50%). However, these rates were 52.63% and 36.36% for AD with anxiety (AD-A) and anxiety disorder, respectively.

Table 1: Characteristics of the psychiatric consultations requested for inpatients diagnosed with Coronavirus 2019 (COVID-19)

Reasons for consultation					Gender distribution*		Duration until consultation request (day)**	
	RC 1 % (n)	RC 2 % (n)	RC 3 % (n)	Total % (n)	Women % (n)	Men % (n)	Mean (SD)	Median (min-max)
Anxiety	18.96 (44)	24.69 (2)	28.57 (2)	15 (48)	19.13 (22)	12.68 (26)	10.09 (10.76)	6.50 (1–54)
Confusion	9.48 (22)	12.34 (10)	-	10 (32)	10.43 (12)	9.76 (20)	7.82 (8.17)	4 (1–32)
Depressive symptoms	6.46 (15)	1.23 (1)	-	5 (16)	10.43 (12)	1.95 (4)	8.60 (6.92)	7 (2–26)
Evaluation for drug–drug interactions	6.03 (14)	1.23 (1)	-	4.69 (15)	6.96 (8)	3.41 (7)	2.07 (0.26)	2 (2–3)
Poor sleep	11.21 (26)	20.98 (17)	28.57 (2)	14.06 (45)	13.91 (16)	14.15 (29)	7.12 (5.96)	4.5 (1–25)
Alcohol–substance use	0.43 (1)	1.23 (1)	-	0.63 (2)	0	0.98 (2)	5	5
Psychomotor agitation	31.46 (73)	11.11 (9)	-	25.63 (82)	18.26 (21)	29.76 (61)	5.89 (6.13)	4 (1–32)
Psychotic symptoms	1.72 (4)	1.23 (1)	14.28 (1)	1.88 (6)	1.74 (2)	1.95 (4)	10.75 (14.88)	4 (2–33)
Death/suicidal ideation	1.29 (3)	3.70 (3)	-	1.88 (6)	0.87 (1)	2.44 (5)	7.33 (5.85)	5 (3–14)
Treatment noncompliance	4.74 (11)	41.97 (34)	28.57 (2)	14.69 (47)	10.43 (12)	17.07 (35)	5 (2.32)	5 (2–9)
Evaluation for somatization	1.72 (4)	1.23 (1)	-	1.56 (5)	2.61 (3)	0.98 (2)	8 (7)	8 (1–15)
Treatment arrangement	6.46 (15)	1.23 (1)	-	5 (16)	5.22 (6)	4.88 (10)	8.60 (9.86)	5 (1–38)
Total	100 (232)	100 (81)	100 (7)	100 (320)	100 (115)	100 (205)	7.19 (7.77)	5 (1–54)

RC: Reason for consultation, * According to all reasons for consultation, ** According to primary reason for consultation

Table 2: Patients' characteristics and clinical features according to psychiatric diagnoses established after evaluation

Psychiatric diagnoses				Gender distribution*		Age*		Duration until consultation request **		Hospital stay**		Past diagnosis*	Medical comorbidity*	ICU*	Death*
	D1 % (n)	D2 % (n)	D3 % (n)	Women % (n)	Men % (n)	Mean (SD)	Median (min-max)	Mean (SD)	Median (min-max)	Mean (SD)	Median (min-max)	% (n)	% (n)	% (n)	% (n)
Anxiety dis.	8.19 (19)	14.29 (3)	8.70 (22)	4.90 (5)	11.26 (17)	58.37 (18.56)	52 (24-89)	13.74 (13.73)	10 (1-54)	23.84 (21.58)	16 (2-84)	68.18 (15)	36.36 (8)	9.09 (2)	4.54 (1)
Bipolar dis.	0.86 (2)	9.52 (2)	1.58 (4)	3.92 (4)	0	44.50 (21.92)	44.5 (29-60)	2.50 (0.71)	2.50 (2-3)	5 (4.24)	5 (2-8)	100 (4)	50 (2)	50 (2)	0
Delirium	31.47 (73)	0	28.85 (73)	23.53 (24)	32.45 (49)	76.41 (11.99)	77 (40-100)	6.41 (6.75)	4 (1–32)	14.99 (9.30)	12 (2–44)	34.24 (25)	75.34 (55)	50.68 (37)	45.20 (33)
Dementia	11.21 (26)	33.33 (7)	13.04 (33)	16.67 (17)	10.60 (16)	79.58 (8.23)	81 (61–91)	2.19 (0.98)	2 (1-5)	16.08 (10.09)	12 (5-37)	100 (33)	45.45 (15)	39.39 (13)	21.21 (7)
Depressive dis.	4.74 (11)	23.81 (5)	6.32 (16)	9.80 (10)	3.97 (6)	60.73 (14.71)	60 (27–80)	7.27 (5.02)	6 (2-20)	11 (6.35)	9 (4–24)	93.75 (15)	62.50 (10)	12.5 (2)	0
İnsomnia dis.	3.88 (9)	0	3.56 (9)	2.94 (3)	3.97 (6)	64.67 (13.80)	67 (48-82)	9.78 (6.94)	8 (4–25)	22.38 (17.97)	14.50 (9-64)	22.22 (2)	55.55 (5)	0	0
Drug side-effect	0.86 (2)	0	0.79 (2)	0	1.32 (2)	68.50 (6.36)	68.50 (64-73)	20.50 (17.67)	20.50 (8–33)	27 (26.87)	27 (8–46)	50 (1)	100 (2)	0	0
Alcohol/substance use disorder	0.86 (2)	4.76 (1)	1.19 (3)	0	1.99 (3)	31 (1.41)	31 (30-32)	3 (2.82)	3 (1-5)	6.50 (0.71)	6.50 (6-7)	100 (3)	0	66.66 (2)	0
Mental retardation	0.86 (2)	0	0.79 (2)	0	1.32 (2)	40 (8.48)	40 (34-46)	2	2	5.50 (2.12)	5.50 (4-7)	100 (2)	0	0	0
Psychotic dis.	3.45 (8)	4.76 (1)	3.56 (9)	3.92 (4)	3.31 (5)	59.13 (15.01)	63.50 (27-72)	2.54 (0.74)	2.50 (2-4)	11.13 (5.69)	8 (6–21)	100 (9)	44.44 (4)	22.2 (2)	0
Somatoform dis.	0.43 (1)	0	0.40 (1)	0	0.66 (1)	88	-	18	-	32	-	100 (1)	100 (1)	0	0
Adjustment dis. (anx)	23.71 (55)	9.52 (2)	22.53 (57)	19.61 (20)	24.50 (37)	57.84 (16.32)	57 (28-88)	8.13 (7.57)	6 (1-35)	17.60 (12.44)	14 (1-54)	19.29 (11)	52.63 (30)	28.07 (16)	10.52 (6)
Adjustment dis. (depr)	7.33 (17)	0	6.72 (17)	10.78 (11)	3.97 (6)	61.18 (16.50)	64 (24-85)	8.41 (6.50)	6 (2-26)	21.71 (13.50)	21 (5-49)	23.52 (4)	76.47 (13)	17.64 (3)	5.88 (1)
No psychiatric diagnosis	2.16 (5)	0	1.98 (5)	3.92 (4)	0.66 (1)	67.80 (20.46)	72 (33-87)	6 (5.24)	4 (2-15)	16.80 (17.19)	12 (3-45)	20 (1)	60 (3)	60 (3)	60 (3)
Total	100 (232)	100 (21)	100 (253)	100 (102)	100 (151)										

D: Diagnosis, ICU: Intensive care unit, * According to all diagnoses, ** According to primary diagnosis

Table 3: Reciprocal distributions of the reasons for consultation according to psychiatric diagnoses and diagnoses according to reasons for consultation

Diagnosis		No diagnosis		Anxiety dis.		Bipolar dis.		Delirium		Dementia		Depressive dis.		Insomnia dis.		Drug side effect		Alcohol-substance use dis.		Mental retardation		Psychotic dis.		Somatoform dis.		Adjustment dis. (anx)		Adjustment dis. (depr.)	
Reason		→ Reasons for consultations according to psychiatric diagnoses (%)→																											
Anxiety	↓ Diagnoses according to reasons for consultation →	0	0	29.4	55.6	0	0	3.9	1.9	2.0	2.2	3.9	9.1	0	0	0	0	0	0	0	0	0	0	0	0	56.9	36.3	3.9	7.7
Confusion		0	0	0	0	0	0	75.7	26.4	16.2	13.3	0	0	0	0	0	0	2.7	20	0	0	2.7	7.7	0	0	2.7	1.3	0	0
Depressive symptoms		6.3	20	0	0	0	0	0	0	0	0	18.8	13.6	6.3	10	0	0	0	0	0	0	0	0	0	0	0	0	68.8	42.3
Evaluation for drug-drug interaction		0	0	0	0	5.0	25.0	0	0	70.0	31.1	15.0	13.6	0	0	0	0	0	0	5.0	33.3	0	0	0	0	5.0	1.3	0	0
Poor sleep		0	0	8.5	14.8	0	0	2.1	0.9	2.1	2.2	10.6	22.7	19.2	90	0	0	0	0	0	0	0	0	0	0	44.7	26.3	12.8	23.1
Alcohol-substance use		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	66.7	40	0	0	33.3	7.7	0	0	0	0	0	0
Psychomotor agitation		2.27	40	3.4	11.1	0	0	58.0	48.1	15.9	31.1	2.3	9.1	0	0	0	0	0	0	1.1	33.3	2.3	15.4	1.1	100	11.4	12.5	2.3	7.7
Psychotic symptoms		0	0	0	0	0	0	33.3	1.9	16.7	2.2	0	0	0	0	16.7	50	0	0	0	0	33.3	15.4	0	0	0	0	0	0
Death/suicidal ideation		0	0	12.5	3.7	12.5	25.0	0	0	0	0	12.5	4.6	0	0	0	0	0	0	0	0	0	0	0	0	37.5	3.8	25.0	7.7
Treatment noncompliance		2.0	20	2.0	3.7	0	0	42.0	19.8	16.0	17.8	4.0	9.1	0	0	0	0	0	0	2.0	33.3	4.0	15.4	0	0	22.0	13.8	6.0	11.5
Evaluation for somatization		16.7	20	0	0	16.7	25.0	0	0	0	0	0	0	0	0	16.7	50	0	0	0	0	0	0	0	0	50	3.8	0	0
Treatment arrangement		0	0	17.7	11.1	5.9	25.0	5.9	0.9	0	0	23.5	18.2	0	0	0	0	11.8	40	0	0	29.4	38.5	0	0	5.9	1.3	0	0

The white lines (from left to right) show the distribution of the reasons for consultation according to the diagnoses, and the gray columns (from top to bottom) show the distribution of the diagnoses according to the reasons for the consultation.

Table 4: Correlations between demographics, clinical features, and outcomes

		1. Age	2. Gender	3. Duration until consultation	4. Hospital stay	5. Past psychiatric diagnosis	6. Medical comorbidity	7. Delirium	8. Intensive care admission	9. Death
1. Age	r_s	-								
	P	-								
2. Gender (f-m)	r_s	0.022	-							
	P	0.744	-							
3. Duration until consultation	r_s	-0.166[c]	0.129[a]	-						
	P	0.011	0.049	-						
4.Hospital stay	r_s	0.088	0.118	0.472[c]	-					
	P	0.183	0.076	<0.001	-					
5. Past psyciatric diagnosis (-/+)	r_s	0.183[b]	-0.094	−0.302[c]	-0.147[a]	-				
	P	0.005	0.155	<0.001	0.027	-				
6. Medical comorbidity (-/+)	r_s	0.215[b]	0.002	0.095	0.045	-0.040	-			
	P	0.001	0.981	0.148	0.503	0.541	-			
7. Delirium (-/+)	r_s	0.385[c]	0.082	–0.075	-0.041	−0.150[a]	0.197[b]	-		
	P	<0.001	0.212	0.252	0.536	0.022	0.003	-		
8. Intensive care admission (-/+)	r_s	0.142[a]	0.063	0.037	0.255[c]	–0.075	0.044	0.260[c]	-	
	P	0.031	0.338	0.573	<0.001	0.253	0.503	<0.001	-	
9. Death (-/+)	r_s	0.229[c]	0.101	–0.005	0.090	–0.101	0.210[b]	0.410[c]	0.685[c]	-
	P	<0.001	0.125	0.940	0.173	0.125	0.001	<0.001	<0.001	-

Significant correlations are shown in bold font. [a] $P<0.05$, [b] $P<0.01$, [c] $P<0.001$.

Relationships between reasons for consultation and psychiatric diagnoses

Table 3 shows the reciprocal distribution of the reasons for consultations reported by the treating physicians and the diagnoses established by the consultant psychiatrist after the evaluation. Accordingly, delirium was diagnosed in 75.68% of the cases who had a consultation due to confusion and in 57.95% of those who were reported to exhibit psychomotor agitation. On the other hand, confusion was reported in 26.42% and psychomotor agitation in 48.11% of the cases diagnosed with delirium. Moreover, delirium was diagnosed in 42% of the cases reported to exhibit treatment non-compliance and in 33.33% of those with reported psychotic symptoms. The most common reasons for consultation for patients diagnosed with psychotic disorder were a request for treatment arrangement (38.46%) and psychomotor agitation and treatment non-compliance (15.38% for both). Finally, 70% of the requests for evaluation of drug–drug interactions involved patients with dementia.

Characteristics of treatment protocols

Notably, psychopharmacological treatment was started in 83.6% (n = 194) of the patients after the psychiatric evaluation. Accordingly, antipsychotic (AP) agents were used in 128 individuals, benzodiazepines (BZD) in 34 subjects, and antidepressants in 54 subjects with combination therapy being used in 10.83% of the patients. In terms of diagnoses, the most frequently adopted protocol for patients with delirium was AP monotherapy (91.42%). Haloperidol was the most frequently prescribed agent (n = 40) followed by an AP-BZD combination (7.14% using lorazepam in all cases). It was found that among those who were diagnosed with AD, 55.93% were started on antidepressants, 32.20% on APs, and 23.72% on BZDs, with a remarkable difference in the treatment choice between AD-A and AD-D. For the whole AD group, mirtazapine (48.48%) was the most frequently prescribed antidepressant followed by selective serotonin reuptake inhibitors (SSRIs) at 30.30%, whereas quetiapine (55.55%) and lorazepam (73.33%) were the most preferred AP and BZD agents, respectively. As for the patients with dementia (mostly treated for symptoms such as psychomotor agitation), 78.94% were started on APs (most frequently olanzapine) and 31.57% on BZDs (most frequently lorazepam) as monotherapy or in combination. It was also seen that among those diagnosed with anxiety disorders, 50% were started on antidepressants (most frequently escitalopram), 38.88% on APs (most frequently quetiapine), and 33.33% on BZDs (most frequently lorazepam) as monotherapy or in combination. Regarding the remaining less common diagnoses, patients with depressive disorder were most frequently started on antidepressants (77.77%) and SSRIs in particular, whereas quetiapine monotherapy was the most preferred regimen (66.66%) for insomnia.

Relationships between the disease course and clinical features

The mean hospital stay of the patients was 16.88 (12.71) days (median = 13). The longest durations were recorded in patients diagnosed with anxiety disorder with 23.84 (21.58) days (median = 16) and insomnia with 22.38 (17.97) days (median = 14.50), while the shortest durations were found for patients with bipolar disorder with 5 (4.24) days (median = 5) and mental retardation with 5.50 (2.12) days (median = 5.50). It was seen that 31.46% (n=73) of the patients had the need for IC during the treatment course. The rate of IC unit admission in women was found to be significantly lower than in men (27.77% versus 33.80%; P=0.001). In terms of diagnoses, 50.68% of the patients diagnosed with delirium, 28.07% of those diagnosed with AD-A, and 17.64% of those diagnosed with AD-D had a history of ICU admission (Table 2).

It was found that 20.69% (n = 48) of the patients who underwent psychiatric consultation died during their stay in the hospital with the mortality rate being significantly lower in women than in men (15.55% versus 24.46%; P=0.001). Of note, the highest mortality rate (60%) was recorded in a small number of patients who underwent consultation due to treatment non-compliance (such as unwillingness to wear an oxygen mask) but were not diagnosed with a psychiatric condition at the end. Not surprisingly, among those with an established psychiatric diagnosis, the highest mortality was observed in the delirium group (45.20%). Again, 67.12% of those with delirium were males, and the mortality rate among male delirium patients was significantly higher than that of women (48.97% versus 37.5%; P=0.003). The rates of delirium and mortality among the patients without a history of chronic diseases were 20% and 10%, respectively, whereas the rates were 38.73% and 27.46%, respectively, for those having medical comorbidities. Similarly, 75.34% of the delirium cases and 81.25% of the deceased patients had at least one medical comorbidity.

Correlations between variables of interest

Inter-correlations are shown in Table 4. The duration from admission to psychiatric consultation positively correlated with the length of hospital stay and negatively correlated with having a past medical history of psychiatric diagnosis (P<0.001 for both). Notably, a history of psychiatric diagnosis was also associated with a shorter hospital stay and a lower rate of delirium (P=0.027 and 0.022, respectively). Not surprisingly, the presence of medical comorbidities, delirium, need for IC, and death during the treatment course were strongly inter-correlated.

Temporal course of the consultation requests and the distribution of psychiatric diagnoses

In terms of the monthly distribution of the psychiatric consultations, it can be seen that 25% (n = 58) of the consultations were requested in December 2020, while the lowest number of consultations were recorded during the first months after the hospital had open for service (Figure 1). It was also observed the rate of dementia was highest in June 2020 (62.5%; n = 15), moreover, these patients constituted 45.45% of all dementia cases over a 1-year period. As for delirium, which was relatively infrequent during the first months of the pandemic, the total number of the cases exhibited a significant increase between October and December 2020 with remarkably high rates of 42.85%, 31.25%, and 41.37%, respectively. Following a two-month decline, the increase resumed as of March 2021 reaching a rate of 40.62% (n = 13) by April 2021. Finally, the total number and the rates of patients diagnosed with AD were highest in October and December 2020 (34.37% and 37.93%, respectively).

In terms of the temporal pattern of the use of psychotropic medications, it was observed that the preference for

haloperidol became increasingly significant over time compared to other APs, whereas no such change was evident for the BZDs and antidepressants. As for delirium, for which APs are the most common treatment options, the rate of haloperidol usage gradually increased from 0% (the first four-month period) to a strikingly high percentage of 82.60% by the last four-month period.

Logistic regression for the prediction of death

In the logistic regression analysis, the occurrence of death over the course of COVID-19 treatment was determined as the binary outcome variable of interest (0: lived, 1: deceased). Accordingly, death over the course of treatment was predicted by the presence of delirium (test–retest reliability [TRR] = 7.01, 95% confidence interval [CI] = 3.43–14.32; $P<0.001$) and medical comorbidities (TRR = 2.58, 95% CI = 1.12–5.93; $P=0.026$). Taken together, the regression model predicted survival and death among the patients with an accuracy of 85.3% and 58.3%, respectively ($P<0.001$).

Discussion

The present study aimed to provide a multidimensional view of the psychiatric consultations requested for inpatients admitted to a specialized pandemic hospital with a diagnosis of COVID-19 over a one-year period from the onset of the pandemic in Turkey. The main research objectives were to examine the characteristics of and relationships between several clinical variables, including patients' socio-demographics, the reasons for psychiatric consultation, psychiatric diagnoses and treatment arrangements after evaluation, clinical courses and outcomes of the inpatient treatment, and temporal course of these variables during the pandemic.

Demographics and clinical characteristics

It can be seen that the rate of male patients was significantly higher than females and the mean age of the sample was strikingly high compared to the general CLP practice. These findings are likely to related to the overall demographic profile of the inpatients with COVID-19, given that both male gender and older age are associated with a more severe clinical prognosis and increased need for hospitalization during the pandemic [11–13]. From a broader perspective of "neuropsychiatric disorders", it is seen that the most common premorbid diagnosis among patients was dementia (on the other hand, the reason for consultation and the treatment arrangements was directly linked to dementia only in a minority of these patients). Strikingly, a significant portion of psychiatric consultations regarding patients with dementia were requested in June 2020. A detailed examination of the records revealed that the observed surge was mostly due to the mass hospitalizations of infected elderly patients from nursing homes regardless of their clinical status on the grounds that isolation measures could not be provided in their institutions. Accordingly, the main reasons for psychiatric consultations for these patients mostly consisted of treatment non-compliance, agitation, and/or the evaluation for the drug–drug interactions between the psychotropics and the medications used for the treatment of COVID-19 (especially hydroxychloroquine). On the other hand, the rate of delirium and/or death was remarkably low in these patients. In line with these findings, in their systematic review, Simonetti et al. [14] reported that the most common symptoms among dementia patients with COVID-19 are apathy, anxiety, and agitation, which could all be partially attributed to the effects of hospitalization and long-term social isolation. On the other hand, the high mortality rate (62.2%) reported among dementia patients hospitalized due to a more severe clinical condition (COVID-19 pneumonia, and others) [15] indicates that the prognosis may be detrimental in special subgroups.

Several factors, such as the rapid spread of the disease, increasing pressure on the health system, increase in the knowledge and clinical experience about the disease, and initiation of the vaccination program in elderly patients as of January 2021 seem to have resulted in substantial changes in the clinical profiles of the patients admitted to hospitals. Indeed, as the impact of the pandemic gradually became more and more detrimental, the proportion of the psychiatric consultations requested for patients with a primary diagnosis of dementia decreased, while the rates of delirium and overall mortality exhibited dramatic increases.

One of the strengths of our study is that the reasons for psychiatric consultation (as stated by the treating physicians) and the diagnoses established by the consultant psychiatrist after evaluation were systematically categorized and analyzed as separately parameters. Accordingly, the most common reasons for consultation in our sample were found to be psychomotor agitation, anxiety, treatment non-compliance, insomnia, and confusion. After psychiatric evaluation, approximately three-fourths of all cases were diagnosed with delirium, AD, and/or dementia. This distribution seems consistent with the findings of a few previous studies conducted on smaller samples [10, 16]. Aside from delirium and dementia, which are neuropsychiatric syndromes characterized by neurocognitive dysfunction, the most common psychiatric diagnosis established after hospitalization was found to be AD. Notably, it can be seen that only one-fifth of those diagnosed with ADs had a past medical history of psychiatric disorders, and only 1/7 of them had used psychotropic medications before hospitalization. On the other hand, the majority of those diagnosed with anxiety disorder and/or depression do have a history of psychiatric diagnosis before hospitalization, and more than half had used psychotropic agents. These two diagnoses may therefore not be directly associated with the effects of COVID-19 infection and related stressors for the affected individuals in our sample. Of course, the symptoms associated with premorbid depression and anxiety disorders may have become exacerbated during hospitalization as also supported by previous evidence [17]. Nevertheless, the cross-sectional nature of our study prevents us from drawing any further inference on this matter.

It is noteworthy that approximately three-fourths of those diagnosed with AD met the characteristics of AD-A, which is in line with previous studies indicating that anxiety symptoms are more common than depression among patients with COVID-19 [18]. Indeed, physical problems caused by the disease and/or the treatment (dyspnea, intubation, and others.), challenging conditions specific to treatment (social isolation, uncertainty about the disease and treatment efficacy, and others), and the flow of distressing information in the media (high mortality rates, among others) might potentially elicit further anxiety and

fear of death among patients [19, 20]. In a prospective cohort study conducted with 44 patients with COVID-19, an increase in anxiety and depression scores was reported in 36% and 29%, respectively, of the patients as per the admission. The rates for high anxiety and depression decreased to 9% and 20%, respectively, after two weeks of follow-up [21].

Another striking finding is that the rate of medical comorbidity was significantly higher in patients diagnosed with AD-D or depressive disorder than in those diagnosed with AD-A or anxiety disorder. Similarly, the rates of AD-D and depressive disorder among those with a medical comorbidity were two and three times higher, respectively, than in the group without such a comorbidity. Although causal underpinnings of this observation extend beyond the scope of our study, the finding is consistent with previous literature in the sense that chronic medical comorbidities have been strongly associated with depression [22, 23].

The findings of our study additionally indicate that insomnia might stand as another common psychiatric condition that is in close association with COVID-19 and/or hospitalization. Indeed, several studies indicate that insomnia stands out as a common clinical condition associated with COVID-19, especially among inpatients [24, 25]. One possible mechanism for the insomnia might be irregular circadian rhythms caused by the disease, treatment process, and/or protective measures [18, 26]. A recent study reported that 40% of 402 inpatients with the diagnosis of COVID-19 exhibited clinically significant insomnia symptoms by the first month after discharge [27]. A multicenter cohort study from the United States found that insomnia was among the most frequent newly diagnosed psychiatric disorders occurring within 14 to 90 days after the disease [18]. Finally, a meta-analysis of 31 studies on the prevalence of psychiatric symptoms in patients with COVID-19 found that the prevalence for sleep disorders was 34% [28].

Our findings show that a relatively small number of the consulted patients had a premorbid diagnoses other than anxiety/depressive disorders, namely patients with bipolar disorder, psychotic disorders, mental retardation, and ASUD collectively constitute a small portion (7.5%) of the diagnoses established after evaluation. Notably, a substantial proportion of the reasons for consultation in these patients consisted of requests for treatment arrangements, evaluation for drug–drug interactions, and treatment non-compliance. Some case reports in the literature suggest that isolated manic or psychotic episodes might occur due to COVID-19 infection although a causal link between COVID-19 and bipolar/psychotic disorders has not been established [29–31]. Of note, no such case was present in our sample.

Treatment non-compliance has become an important agenda in the COVID-19 wards. Indeed, adherence to the strict treatment protocols can be extremely challenging for many patients. In our sample, psychomotor agitation and/or treatment non-compliance were cited as the reasons for psychiatric consultation in approximately one-third of the patients diagnosed with psychotic disorders, two-thirds of those with mental retardation, and nearly half of the patients with dementia. It has been reported that patients with psychosis experience more problems in complying with preventive measures and treatment protocols, and that these patients are more reluctant to accept vaccinations and isolation protocols [32]. Similarly, patients with mental retardation are also reported to be at increased risk of abuse due to their difficulties in understanding and adapting to special requirements [33]. From this point-of-view, it seems imperative for policy makers to develop multidimensional strategies to include care institutions, social service units, non-governmental organizations, and healthcare workers to increase treatment compliance among these vulnerable subgroups [34].

Treatment protocols

It is noteworthy that some agents were more frequently prescribed than others in the same class and that the preference pattern varied within the temporal course of the pandemic. During the pandemic, many psychiatrists working in the field of CLP had to make critical decisions and needed to improve their knowledge about specific medications (hydroxychloroquine, tocilizumab, favipiravir, remdesivir, azithromycin, and others) in addition to possible drug interactions that they were aware of at an anecdotal level [35, 36]. For example, in the early periods when hydroxychloroquine was extensively used for treatment, the use of haloperidol was largely avoided (possibly due to the risk of cardiological side effects and interactions). However, it was observed that the preference for olanzapine turned in favor of haloperidol as treatment protocols and patient profiles changed over time. Indeed, olanzapine is known for its anticholinergic side effects that have been associated with an increase in delirium severity in elderly hospitalized patients [37, 38]. Again, mirtazapine, sertraline, and escitalopram, which were the most preferred antidepressants, and lorazepam, which was the most commonly administered BZD in our sample, stand out as plausible treatment options that are mostly in line with the recommendations of the corresponding guidelines [39, 40].

In our study, the fact that the shortest durations for psychiatric consultations were associated with psychomotor agitation and treatment non-compliance might reflect the hierarchy of requirements in the pandemic wards in which compliance with treatment protocols and preventive measures are of vital importance. In this context, determining the early needs of all hospitalized patients, increasing treatment compliance, planning preventive approaches, and providing psychoeducation stand out as highly important aspects of CLP practice during the pandemic [41, 42].

Delirium and death

Not surprisingly, the highest rates of intensive care requirements and mortality were recorded among the patients diagnosed with delirium [20]. Findings from different studies indicate that the incidence of delirium in patients diagnosed with COVID-19 varies between 9% and 14.8% [43, 44]. The logistic regression model created with the variables examined in our study showed that delirium and medical comorbidities were the strongest predictors of death among COVID-19 patients who underwent psychiatric consultation. Similarly, a study conducted on 707 inpatients in Brazil reported delirium as an independent predictor of hospital deaths due to COVID-19 in patients over 50 years of age [45]. In another study conducted in Spain, delirium and a history of mood disorder were associated with high mortality [46]. In this regard, early recognition of delirium in COVID-19 patients (in our study, a significant proportion of the

patients diagnosed with delirium were consulted for non-specific reasons other than confusion), and consideration of the most appropriate treatment options on an individual basis still constitute a critical agenda in CLP practice in hospitals.

Strengths and Limitations

The findings of our study should be approached within the framework of several methodological limitations. The fact that the sample consisted only of patients who underwent psychiatric consultation limits the generalizability of the findings concerning the characteristics of neuropsychiatric symptoms and the rates of psychiatric disorders among inpatients with COVID-19. Considering that the number of inpatients admitted to our hospital was around 6000 over the first one-year period, it is likely that the incidence of these conditions might actually be higher than reflected in psychiatric consultations. Furthermore, due to the fact that a large number of psychiatry residents have been assigned as ward physicians during the pandemic, many clinical situations might have been handled without being subject to official psychiatric consultations through the hospital's medical record system. Another limitation is that information about the dose and duration of the treatments were not included in the data analysis due to technical restrictions.

On the other hand, the fact that the present findings and observations on psychiatric consultations reflect the general profile of COVID-19 patients treated in one of the largest pandemic hospitals in our country, the inclusion of several well-defined clinical variables in the multidimensional analyses and the emphasis on the temporal course of these variables throughout the one-year period from the onset of the pandemic stand out as the strengths and distinguishing features of our study. In addition, systematic and multi-level classification of the variables of interest (such as the reasons for consultation and post-evaluation diagnoses under separate headings) and the distinction between clinical entities (such as the subtypes of AD) might contribute to a better understanding of the relationship between the observed symptoms and underlying clinical diagnoses.

Conclusion

As in other fields of public health, the COVID-19 pandemic has caused a detrimental and multi-faceted impact on psychiatric treatment services. Neuropsychiatric symptoms and syndromes associated with the disease have become a focus of interest during daily CLP practice in several institutions, such as in the pandemic hospitals, in which inpatient COVID-19 treatment is delivered. In the present case, our findings collectively indicate that AD and delirium were the two most common diagnoses among COVID-19 patients who underwent psychiatric consultations during the first year of the outbreak. It should also be noted that the characteristics of the consultations and the treatment preferences exhibited significant variability over the course of the pandemic.

During the ongoing struggle against COVID-19, the knowledge and experience gained in the field of CLP might contribute to the recognition of disease-related neuropsychiatric syndromes and the implementation of appropriate treatment interventions in the coming years. We also believe that the treatment experiences gained with COVID-19 patients having severe mental disorders might provide guidance for the development of specialized treatment strategies and social policies to target these specific groups.

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