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# Treatment of mental disorders and the course of COVID-19

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## ABSTRACT

**Introduction:** Psychiatric patients are an interesting group due to the risk of mental exacerbation during COVID-19 (coronavirus disease 2019). Most patients with severe mental disorders require long-term care in specialized centres. As a result, such patients are at increased risk of acquiring infectious diseases, including COVID-19. This study evaluated the potential association between mental disorder treatment and the course of COVID-19.

**Material and methods:** The study is a retrospective analysis of data collected from 107 men with mental disorders, aged 30–82 years, inhabitants of nursing homes who have been receiving drugs acting on the central nervous system for at least one year and were diagnosed with COVID-19 between September 2020 and January 2021.

**Results:** More than 80% of patients experienced elevated body temperature during COVID-19. 11 patients required hospitalization due to severe COVID-19 course; one of them died. The most common mental disorder diagnosis included schizophrenia, schizotypal and delusional disorders, and mental retardation. A significantly higher frequency of increased body temperature was observed in patients treated with anxiolytics (particularly in the subgroup who received hydroxyzine treatment).

**Conclusions:** The course of COVID-19 was mild in most patients (almost 90% of the studied population) and did not negatively affect their mental condition. Special care received by the patients resulted in early diagnosis of COVID-19 and a very low mortality rate. Treatment with hydroxyzine significantly influenced the incidence of increased body temperature during the course of COVID-19.

**Keywords:** Mental disorders, COVID-19, antipsychotics, schizophrenia, anxiolytics

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## Introduction

COVID-19 (coronavirus disease 2019) has many symptoms, including acute and post-acute neuropsychiatric sequelae such as headache, anosmia, and dysgeusia. Moreover, cognitive impairment symptoms (short-term memory loss, concentration problems, word-finding problems, and impaired daily problem-solving) were observed among symptomatic COVID-19 patients [1]. Although recent data showed no differences concerning psychiatric diagnosis and neuropsychiatric symptoms between COVID-19 survivors and controls, significantly worse cognitive outcomes were still found among survivors of COVID-19 [2]. The exact mechanism of COVID-19 neuropsychiatric sequelae is still unclear; however, neuropsychiatric symptoms correlate with serum inflammatory markers concentration [3].

Psychiatric patients are an interesting group due to the risk of mental exacerbation during the course of COVID-19 [4]. Most patients with severe mental disorders require long-term care in specialized centres such as psychiatric hospitals and nursing homes. As a result, such patients are at increased risk of acquiring infectious diseases, including COVID-19 [5]. Additionally, they often have concomitant disorders, such as hypertension, diabetes, obesity, metabolic syndrome, and dyslipidaemia, which contribute to the severe course of COVID-19 [6–9]. Scientific data confirmed the increased incidence of COVID-19 in patients with mental disorders [10–11].

It is worth noting that recent data revealed an increasing number of mental and behavioural disorders in Poland [12]. Therefore, the present study aimed to evaluate the potential association between mental disorder treatment and the course of COVID-19.

**Table 1.** Characteristics of the patients

<b>Mean age (SD, standard deviation) [years]</b>		<b>56.52 (12.21)</b>
Body temperature [number of patients (per cent)]	< 37°C	21 (19.63%)
	37–38°C	44 (41.12%)
	> 38°C	42 (39.25%)
COVID-19 [number of patients (per cent)]	Hospitalizations	11 (10.28%)
	Deaths	1 (0.93%)
Diagnosis [number of patients (per cent)]	Cerebral palsy and other paralytic syndromes (G80–G81)	14 (13.08%)
	Episodic and paroxysmal disorders (G10–G17)	22 (20.56%)
	Mental retardation (F70–F79)	42 (39.25%)
	Mood [affective] disorders (F10–F19)	1 (0.93%)
	Organic, including symptomatic mental disorders (F00–F09)	24 (22.43%)
	Schizophrenia, schizotypal and delusional disorders (F10–F19)	47 (43.93%)
	Concomitant diseases [number of patients (per cent)]	Acute coronary syndrome
	Acute viral hepatitis b and a	1 (0.93%)
	Anaemia	9 (8.41%)
	Angina/angina pectoris	3 (2.80%)
	Arrhythmia	1 (0.93%)
	Atopic dermatitis	1 (0.93%)
	Cholelithiasis	1 (0.93%)
	Diabetes	14 (13.08%)
	Dyslipidaemia	8 (7.48%)
	Heart failure	5 (4.67%)
	Hypertension	28 (26.17%)
	Hyperuricemia	3 (2.80%)
	Peptic ulcer disease	3 (2.80%)
	Prostate hyperplasia	4 (3.74%)
	Psoriasis	2 (1.87%)
	Urinary incontinence	6 (5.61%)

## Material and methods

The study is a retrospective analysis of data collected from 107 men with mental disorders, aged 30–82 years, inhabitants of nursing homes in Wielkopolskie voivodeship. All of them have been receiving drugs acting on the central nervous system for at least one year and were regularly monitored concerning the treatment's safety. Clinical and treatment information was obtained from patients' files. All patients were diagnosed with COVID-19 between September 2020 and January 2021. None of the patients received vaccination against SARS-CoV-2. Mental disorder treatment was not modified during the course of COVID-19.

The patients were divided into groups according to the treatment received (ATC/DDD Index 2022) and

mental disorders diagnosed. Statistical analysis was carried out using Statistica 13.3 (TIBCO Software Inc.). The p-value < 0.05 was considered statistically significant. Pearson's chi-square test (with Yates correction for cases with expected frequencies < 5) was used to assess the statistically significant difference between studied groups.

## Results

A primary characteristic of the studied population is presented in Table 1. More than 80% of patients experienced elevated body temperature during the course of COVID-19. 11 patients (10.28% of the population) required hospitalization due to severe COVID-19 course;

**Table 2.** Drugs used in the treatment of mental disorders. Classification according to ATC

Treatment	Number of treated patients [%]
<b>Anticholinergic agents:</b> biperiden	33 (30.84)
<b>Anti-dementia drugs:</b> donepezil, memantine	2 (1.87)
<b>Antidepressants:</b> amitriptyline, citalopram, sertraline, mianserin, trazodone	18 (16.82)
<b>Antiepileptics:</b> clonazepam, carbamazepine, valproate + valproic acid, gabapentin, lamotrigine, levetiracetam	57 (53.27)
<b>Antipsychotics:</b> levomepromazine, perazine, haloperidol, chlorprothixene, zuclopenthixol, clozapine, olanzapine, quetiapine, amisulpride, tiapride, lithium, risperidone, aripiprazole	89 (83.18)
<b>Anxiolytics:</b> alprazolam, diazepam, lorazepam, hydroxyzine	27 (25.23)
<b>Hypnotics and sedatives:</b> estazolam, nitrazepam	9 (8.41)
<b>Other nervous system drugs:</b> cinnarizine	2 (1.87)
<b>Psychostimulants, agents used for ADHD and nootropics:</b> vinpocetine	6 (5.61)

one of them died (0.93% of the population). All patients' diagnoses were categorized according to ICD-10. Most of the patients (83.18%) had schizophrenia, schizotypal and delusional disorders (43.93%), and mental retardation (39.25%) as primary clinical diagnoses.

Antipsychotics and antiepileptics were the most commonly used drugs in the studied population (Tab. 2). No worsening of the mental condition was noted after recovery from COVID-19.

The analysis of associations between received treatment, body temperature, and COVID-19 hospitalization revealed statistically significant differences for patients treated with anxiolytics (higher frequency of elevated body temperature). The results are presented in Tables 3 and 4.

The patients treated with anxiolytics received drugs from one of two pharmacological subgroups: benzodiazepine derivatives (alprazolam, clonazepam, lorazepam, diazepam) or diphenylmethane derivatives (hydroxyzine). Statistical analysis revealed a significant association with increased body temperature only for patients treated with hydroxyzine (Tab. 5).

Table 6 presents the list of drugs (used by some patients in the studied population) that have been reported as associated with temperature dysregulation, leading to hypothermia. However, no differences were observed between patients treated and not treated with these drugs concerning elevated body temperature (Tab. 7).

## Discussion

Mental disorders are chronic diseases often requiring psychotherapy and significant care from family and mental health care providers besides specific pharmacotherapy [13]. The COVID-19 pandemic significantly

contributed to the worsening of the world's population's mental health [14]. A lot of scientific data indicate that patients with mental disorders are at increased risk of severe course and mortality of COVID-19 [11, 15–19]. Li et al. [15] observed a higher mortality rate in patients with a psychiatric diagnosis than those without mental disorders (35.7% vs. 14.7% in the 2-week mortality and 40.9% vs. 22.2% in the 3-week mortality rate). A nationwide Korean study on more than 200,000 patients tested for SARS-CoV-2 concluded that the presence of severe mental illness posed a slightly higher risk of severe COVID-19 course compared to patients without psychiatric diagnosis [11]. A paper from Nemani et al. revealed a significant association between schizophrenia spectrum disorders and COVID-19 mortality, while no such association was confirmed for mood or anxiety disorders [16]. Toubasi et al. carried out a meta-analysis including 634,338 COVID-19 patients from 16 studies, which resulted in higher mortality observed among schizophrenia, schizotypal, and delusional disorders patients compared to mood disorders patients [17]. Another meta-analysis by Fond et al. [18], based on 16 observational studies in 7 countries, recruiting 19 086 patients, further confirmed an increased COVID-19 mortality rate among patients with mental health disorders. A meta-analysis of 10 studies with 263,207 COVID-19 patients not only resulted in an association between schizophrenia and increased COVID-19 mortality but also revealed that the mortality among such patients was significantly influenced by older age and smoking [19].

Increased risk of acquiring COVID-19 by patients with mental disorders may be caused by several factors, including cognitive impairment, little awareness of risk, and problems with effective infection control in

**Table 3.** Analysis of potential association between received treatment and body temperature. Data presented as number of patients (percentage)

Treatment	Body temperature		Total	P-value
	< 37°C	≥ 37°C		
<b>Anticholinergic agents</b>				
No	18 (24.32%)	56 (75.68%)	74	0.518
Yes	10 (30.30%)	23 (69.70%)	33	
Total	28	79	107	
<b>Anti-dementia drugs</b>				
No	28 (26.67%)	77 (73.33%)	105	0.398
Yes	0 (0.00%)	2 (100.00%)	2	
Total	28	79	107	
<b>Antidepressants</b>				
No	24 (26.97%)	65 (73.03%)	89	0.902
Yes	4 (22.22%)	14 (77.78%)	18	
Total	28	79	107	
<b>Antiepileptics</b>				
No	17 (34.00%)	33 (66.00%)	50	0.084
Yes	11 (19.30%)	46 (80.70%)	57	
Total	28	79	107	
<b>Antipsychotics</b>				
No	4 (22.22%)	14 (77.78%)	18	0.678
Yes	24 (26.97%)	65 (73.03%)	89	
Total	28	79	107	
<b>Anxiolytics</b>				
No	26 (32.50%)	54 (67.50%)	80	0.011*
Yes	2 (7.41%)	25 (92.59%)	27	
Total	28	79	107	
<b>Hypnotics and sedatives</b>				
No	26 (26.53%)	72 (73.47%)	98	0.909
Yes	2 (22.22%)	7 (77.78%)	9	
Total	28	79	107	
<b>Other nervous system drugs</b>				
No	28 (26.67%)	77 (73.33%)	105	0.970
Yes	0 (0.00%)	2 (100.00%)	2	
Total	28	79	107	
<b>Psychostimulants, agents used for ADHD and nootropics</b>				
No	26 (25.74%)	75 (74.26%)	101	0.947
Yes	2 (33.33%)	4 (66.67%)	6	
Total	28	79	107	

\*Statistical significance at P &lt; 0.05

psychiatric wards [20]. It is consistent with the present observations — all inhabitants of studied nursing homes got infected with SARS-CoV-2 (confirmed with the antigen

test). One of the diseased patients died from COVID-19, which constitutes 0.93% of the studied population and 2.13% of patients with schizophrenia, schizotypal, and

**Table 4.** Analysis of potential association between received treatment and COVID-19 hospitalization. Data presented as number of patients (percentage)

Treatment	COVID-19 hospitalization			P-value
	No	Yes	Total	
<b>Anticholinergic agents</b>				
No	69 (93.24)	5 (6.76%)	74	0.146
Yes	27 (81.82)	6 (18.18%)	33	
Total	96	11	107	
<b>Anti-dementia drugs</b>				
No	94 (89.52)	11 (10.48)	105	0.489
Yes	2 (100.00)	0 (0.00%)	2	
Total	96	11	107	
<b>Antidepressants</b>				
No	81 (91.01%)	8 (8.99%)	89	0.580
Yes	15 (83.33%)	3 (16.67%)	18	
Total	96	11	107	
<b>Antiepileptics</b>				
No	45 (90.00%)	5 (10.00%)	50	0.929
Yes	51 (89.47%)	6 (10.53%)	57	
Total	96	11	107	
<b>Antipsychotics</b>				
No	16 (88.89%)	2 (11.11%)	18	0.766
Yes	80 (89.89%)	9 (10.11%)	89	
Total	96	11	107	
<b>Anxiolytics</b>				
No	73 (91.25%)	7 (8.75%)	80	0.596
Yes	23 (85.19%)	4 (14.81%)	27	
Total	96	11	107	
<b>Hypnotics and sedatives</b>				
No	90 (91.84%)	8 (8.16%)	98	0.071
Yes	6 (66.67%)	3 (33.33%)	9	
Total	96	11	107	
<b>Other nervous system drugs</b>				
No	95 (90.48%)	10 (9.52%)	105	0.489
Yes	1 (50.00%)	1 (50.00%)	2	
Total	96	11	107	
<b>Psychostimulants, agents used for ADHD and nootropics</b>				
No	90 (89.11%)	11 (10.89%)	101	0.872
Yes	6 (100.00%)	0 (0.00%)	6	
Total	96	11	107	

delusional disorders; in comparison, COVID-19 mortality in the whole Polish population is 1.85% [21]. It is worth underlining that the patient had concomitant disorders (arrhythmia and hypercholesterolemia).

The most important factors increasing the risk of COVID-19 death in patients with schizophrenia include physical health problems, socioeconomic status, social isolation, discrimination, delay in seeking treatment,

**Table 5.** Analysis of the potential association between received treatment and body temperature for patients treated with benzodiazepine derivatives or diphenylmethane derivatives (hydroxyzine)

Treatment	Body temperature			P-value
	< 37°C	≥ 37°C	Total	
<b>Benzodiazepine derivatives</b>				
No	26 (27.66%)	68 (72.34%)	94	0.544
Yes	2 (15.38%)	11 (84.62%)	13	
Total	28	79	107	
<b>Diphenylmethane derivatives (hydroxyzine)</b>				
No	28 (30.11%)	65 (69.89%)	93	0.039*
Yes	0 (0.00%)	14 (100%)	14	
Total	28	79	107	

Data presented as number of patients (percentage). \*Statistical significance at  $P < 0.05$

**Table 6.** Drugs associated with hypothermia used in the studied population

Drug name	Number of patients [%]
Amisulpride	3 (2.80)
Aripiprazole	1 (0.93)
Chlorprothixene	2 (1.87)
Clozapine	13 (12.15)
Haloperidol	7 (6.54)
Levomepromazine	26 (24.30)
Olanzapine	18 (16.82)
Quetiapine	15 (14.02)
Risperidone	16 (14.95)
Sulpiride	2 (1.87)
Tiapride	4 (3.74)
Zuclopenthixol	7 (6.54)

and restricted healthcare access [19, 22]. The mortality observed in the study population was relatively low compared to other studies [17–19]. It can be explained by specific care received by the patients. All of them were inhabitants of nursing homes. Their condition was monitored by qualified staff, and any symptoms indicating SARS-CoV-2 infection resulted in immediate treatment. Such factors as social isolation, seeking treatment delay, or restricted healthcare access were no longer an issue there.

It is known that antipsychotic treatment can result in abnormal changes in body temperature [23]. The possible mechanism includes drugs' action on D2 dopamine receptors and 5-HT<sub>2</sub> serotonin receptors [24]. For example, antagonism of the 5-HT<sub>2</sub> receptor may

**Table 7.** Analysis of potential association between increased body temperature and drugs associated with hypothermia. Data presented as number of patients (percentage)

Drugs associated with hypothermia	Body temperature			P-value
	< 37°C	≥ 37°C	Total	
No	6 (19.35%)	25 (80.65%)	31	0.306
Yes	22 (28.95%)	54 (71.05%)	76	
Total	28	79	107	

lead to hypothermia associated with some antipsychotics [25]. No such adverse effects were observed in the study population. However, it was observed that patients treated with hydroxyzine were significantly more likely to develop increased body temperature during the course of COVID-19. It is worth underlining that the observation might be biased by the relatively small population studied (108 patients; 14 receiving hydroxyzine treatment) — further research on larger groups of patients is necessary to confirm or decline it. The authors did not find any relevant information in the scientific literature discussing such action of hydroxyzine. A paper by Sánchez-Rico et al. [26] revealed that hydroxyzine use was associated with reduced COVID-19 mortality; however, the present sample is too small to draw similar conclusions.

## Conclusion

The course of COVID-19 was mild in most patients (almost 90% of the studied population) and did not

negatively affect their mental condition. Special care received by the patients resulted in early diagnosis of COVID-19 and a very low mortality rate. Treatment with hydroxyzine significantly increased the occurrence of elevated body temperature during the course of COVID-19.

## Article information

**Statement of competing interests:** *The authors declare that they have no competing interests.*

**Ethics statement:** *The study is a retrospective analysis of data from medical documentation. According to the regulations of the Poznan Medical University Bioethics Committee, no ethics-committee approval is necessary in such a situation ([http://www.bioetyka.amp.edu.pl/BADANIA\\_NAUKOWE\\_NIESPONSOROWANE.html](http://www.bioetyka.amp.edu.pl/BADANIA_NAUKOWE_NIESPONSOROWANE.html)). No data allowing for the identification of patients was presented in the publication.*

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