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Methamphetamine Addiction

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ABSTRACT

Objectives: A person can develop an addiction to many kinds of substances. Methamphetamine is the second most widely abused drug worldwide. Long-term methamphetamine usage may cause social, psychological, and physical problems. Long-term effects (such as weight loss, memory loss, tremors, convulsion, psychosis, paranoia, hallucinations, Parkinson's-like symptoms, and cardiovascular collapse) and short-term effects (such as euphoria, dilated pupils, insomnia, reduced appetite, increased blood pressure) are listed and, brain damage and mental problems due to methamphetamine abuse are briefly mentioned in this text. The severity of withdrawal symptoms varies from person to person. Unfortunately, there is no exact cure for methamphetamine abuse. This is not a systematic review.
Keywords: methamphetamine, addiction, brain damage, meth mouth.

Addiction is a chronic dysfunction of brain. It can also be classified as biologic, psychological and social disease. It makes the addict seek for the substance despite of its damages. People can develop an addiction to alcohol, tobacco, hallucinogens (such as LSD), heroin, painkillers, sedatives, hypnotics and tranquilizers, cocaine, methamphetamine and other stimulants. [1] Some symptoms of addiction can be listed as; having a strong need for the substance, starting not to fulfill his/her responsibilities due to using the related substance, continuing to use despite negative consequences, unsuccessful trials to quit, living physical, psychological, social and economic problems due to using the substance, having developed tolerance against the substance, living withdrawal symptoms (nausea, insomnia, anxiety, aggressiveness, diarrhea, shivering, fever, etc.) when not used the substance.

Abuse of the illegal psychostimulant, methamphetamine, which was first synthesized in 1919 as a synthetic substitute for ephedrine has become a worldwide health problem. [2] It is estimated that there are approximately 35 million users; a number which exceeds the total amount of people who are addicted to heroin and cocaine. This makes methamphetamine the second most abused drug; the first widely abused drug is cannabis. [3]

Clinical Effects

Though methamphetamine (as well as amphetamine) is a central nervous system stimulant to treat some diseases such as attention deficit hyperactivity disorder, obesity and narcolepsy, it is also one the addictive's which has a large potential for abuse with long-lasting brain damage and many other problems. [4]

Methamphetamine (commonly known as speed, meth, ice, crystal, or chalk) can be taken by smoking, swallowing, snorting, and injecting a dissolved

powder. It causes a general sense of high mood and well-being. It starts working very fast and its effects can last six to ten hours. [5, 6]

Using methamphetamines have some short-term and long-term effects. Some short-term effects can be listed as enhanced mood and body movement, euphoria, dilated pupils, increased wakefulness, insomnia, reduced appetite, increased blood pressure, rapid and/or irregular heartbeat, hyperthermia, neuropsychiatric symptoms (like anxiety, psychosis, and hallucinations) and cardiovascular collapse. Long-term effects can be listed as changes in brain structure and function (methamphetamine stimulates some neurotransmitters like dopamine, norepinephrine, and serotonin), weight loss, memory loss, tremors, convulsion, psychosis, paranoia, hallucinations, Parkinson's-like symptoms, cardiovascular collapse, which may cause death. In some cases, psychotic symptoms can last for months or years even after the addict stops using methamphetamine. [7-11]

A meta-analysis of the neuropsychological effects of methamphetamine abuse revealed medium size effect; resulting in deficits in episodic memory, executive functions, information processing speed, motor skills, language, and visuoconstructional abilities. [12]

A study was made in Harbor UCLA Medical Center by Dr. Thomas Ernst and Dr. Linda Chang using magnetic resonance spectroscopy. They intended to measure brain chemical levels and aimed to reveal whether the brain cells of methamphetamine abusers were healthy or not. After the study, Dr. Chang clarified that they discovered strong cell damage and abnormal brain chemistry in all brain regions of participants. [13]

Studies made by structural magnetic resonance imaging, single photon emission computed tomography, and proton magnetic resonance spectroscopy have revealed that chronic use of methamphetamine produces malign effects. Positron emission tomography has revealed that (compared with measures of control group participants) methamphetamine addicts have lower levels of dopamine transporters in the striatum and prefrontal cortex and show differences in regional cerebral glucose metabolism. [14-23]

Another unpleasant and also one of the most visible consequence effects that is associated with methamphetamine abuse is extreme tooth decay; called meth mouth. Researchers argue that relevant tooth decay is due to methamphetamine's restriction of salivary flow, which leads to xerostomia (dry mouth). Because xerostomia can increase the likelihood of plaque and dental caries (tooth decay), this condition might underlie the attention-grabbing pictures of meth mouth seen in social media. [24, 25]

Withdrawal Effects

Dysphoric mood is the main symptom of methamphetamine withdrawal, with psychomotor agitation or retardation, vivid, unpleasant dreams, fatigue, insomnia, or in some cases hypersomnia. [26, 27] Depressive symptoms vary in intensity and duration. [28] Some of the less severe withdrawal symptoms are anxiety, motor retardation, agitation, vivid dreams, poor concentration, irritability, and tension decrease at 7-10 days. [29-32] The severity of methamphetamine withdrawal symptomatology is likely to influence the ability of methamphetamine addiction patients to maintain abstinence. [28]

Treatment

Because addicts have a high percentage of dropout and relapse, methamphetamine addiction treatment is troublesome. Addicts' facing with severe psychosis episodes and craving makes the process even harder. [33, 34] There are no specific medicines that can help addict that prolong abstinence from the substance. But there are some medications which are approved by FDA for other side effects and diseases that might be useful in treating methamphetamine addiction. The best plans are comprehensive, which include medications, psychotherapy (including behavioral therapy, family therapy and group therapy) and medical services (to help treat serious complications of addiction like withdrawal during detox period). [8-10, 35, 36] Research also continues in order to developed medicines and other kinds of treatments for methamphetamine abuse, including vaccines and noninvasive stimulation of the brain by using magnetic fields. [37]

CONCLUSION

Methamphetamine abuse is one of widest substance addiction type worldwide. Because of the reason that it is cheap, it is easy to reach. It has detrimental effects in human body, which are proved by technological health devices. There is no medication which can cure methamphetamine addiction. It is important to go on studies to set aside related harmful effects of methamphetamine abuse.

Authors' Contribution

Study Conception: Bİ,; Study Design: Bİ,;

Supervision: ÖG,; Materials: ÖG,; Data Collection and/or Processing: Bİ,; Statistical Analysis and/or Data Interpretation: Bİ,; Literature Review: ÖG,; Manuscript Preparation: Bİ, ÖG and Critical Review: ÖG.

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Evaluation of prognostic factors in febrile neutropenic patients with hematological malignancies

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ABSTRACT

Objectives: Hematological malignancies presenting with febrile neutropenia constitute an important health issue all over the globe. In this study we aimed to elucidate the prognostic factors of febrile neutropenic patients with hematological malignancies and to investigate the causes of mortality.

Method: This research had a retrospective nature. A total of 174 febrile neutropenia patients $\geq$ 18 years of age hospitalized has been enrolled in the study. Patients enrolled in the analy-sis were determined according to American Society for Infectious Diseases 2010 Febrile Neutro-penia Diagnosis and Treatment Guidelines. Accordingly, neutropenia was defined as an expected decrease in the absolute neutrophil count (ANS) to < 500 cells/mm³ or < 500 cells/mm³ over the next 48 hours and body temperature over $\geq$ 38°C.

Results: A total of 174 patients has been included in the analysis and 32 (18.5%) died while 142 (81.5%) did not develop mortality. When the statistically significant results are evaluated according to multivariate analysis; Age, Crp, MASCC, acute renal failure, hypotension were similar in both groups. On the other hand, when univariate statistically highly significant results are evaluated ac-cording to multivariate analysis; Presence of urinary catheter, diagnosis of bacterial pneumonia and ANS not increasing after 1 week were found to be statistically significant in the mortality group.

Conclusion: The results of the study showed that in febrile neutropenic patients, mortality was increased by 6.7 times by a diagnosis of bacterial pneumonia, 245.6 times by the absence of ANS elevation, and 13.9 times by urinary catheterization.

Keywords: Febrile neutropenia, hematological malignancy, mortality

Hematological malignancies presenting with febrile neutropenia constitute an important health issue all over the globe. There has been an increase in the treatment success of patients with hematologi-cal malignancies in recent years with developments in cytotoxic agents. However these molecules have also raised the risk of opportunistic infections. Fever seen in patients with neutropenia after chemotherapy may be the first and often the only symptom of infection. On the contrary, fever may not be observed in the elderly and patients receiving corticosteroid therapy. In such cases, hypoten-sion or clinical deterioration may also be significant in revealing infections.

Nevertheless, non-infectious causes of fever, such as tumor necrosis, bleeding, and drugs with a pyrogen effect should not be overlooked. In neutropenic patients, signs of inflammation may be subtle. Therefore, taking cultures from possible foci of infection in neutropenic patients is very important in

obtaining evidence of infection and guiding treatment. In the presence of prolonged neutropenia and deep neutropenia, the risk of infection increases. Bacterial infection is inevitable in almost all cases with deep neutropenia lasting longer than three weeks. [1]

Severe mucosal damage, especially in the gastrointestinal tract is the most important focus of infec-tion following chemotherapy. The genitourinary system, skin and soft tissue, and respiratory tract are other foci of infection. Bacteremia and invasive fungal infections are common in neutropenic patients whose mucosal barrier has been destroyed, but only 10-25% of these cases can be docu-mented. Approximately 80% of infections identified in many patients are caused by endogenous flora bacteria. [2] However, a significant portion of hospitalized patients are colonized with microor-ganisms in the hospital flora within weeks following their hospitalization. This further increases the possibility of resistant microorganisms in infections that develop during hospitalized care.

Despite all developments up to date, infections remain the most common cause of death in patients with hematological malignancies. [3] While the mortality rate associated with febrile neutropenia was reported to be 30% in the 1970s, it has decreased to 2-10% with advances in antibiotic therapy and early antimicrobial therapy. [4] In the United States, approximately 1 patient dies from hematological malignancy in every nine minutes. Such high mortality rates show the importance of a preemptive approach to these patients. International guidelines recommend taking blood cultures from patients presenting with neutropenic fever and initiating antimicrobial therapy within 60 minutes. [5] Howev-er, some researchers suggest that treatment should be started within 30 minutes. [6] During septic shock, survival is reduced by 8% for each hour of delay in the initiation of therapy. [7] The aim of this study was to determine factors of poor prognosis in patients with febrile neutropenia.

Study Hypothesis

In this study we aimed to elucidate the prognostic factors of febrile neutropenic patients with hema-tological malignancies and to investigate the causes of mortality.

METHODS

This research had a retrospective nature. Febrile neutropenia patients ≥ 18 years of age hospitalized has been enrolled in the study. A total 174 patients diagnosed with hematological malignancies, who received inpatient treatment at the Adult Hematology Clinic of Eskişehir Osmangazi Universi-ty Medical Faculty Hospital between January 2016 and August 2018 has been enrolled in this study. Ethics committee approval has been granted at 18.09.2018 with protocol number 11-09/2018. The study was conducted according to the Declaration of Helsinki clinical research prin-ciples and informed consent form was obtained from all participants.

Patients enrolled in the analysis were determined according to American Society for Infectious Diseases 2010 Febrile Neutropenia Diagnosis and Treatment Guidelines. Accordingly, neutropenia was defined as an expected decrease in the absolute neutrophil count (ANS) to < 500 cells/mm³ or < 500 cells/mm³ over the next 48 hours. Fever was defined as the single oral measurement of body temperature being ≥ 38.3 °C (101 °F) or a persistent level of ≥ 38 °C (100.4 °F) over a one-hour period.

Febrile neutropenia attack, which occurred between the day of hospitalization and discharge, was evaluated once. The daily peak fever, number of days to fever response, and blood values of white blood cell count, ANS, C-reactive protein (CRP) and procalcitonin (PCT) were recorded. The state of consciousness, hypotension, total parenteral nutrition support, and development of mucositis were also noted from the daily follow-up notes. Patients with underlying diseases were examined in terms of mortality.

The patients who were administered granulocyte-colony-stimulating factor (G-CSF) on the day they became febrile neutropenic were noted. The ANS value not exceeding 500 cells/mm³ within one week was considered as the absence of ANS elevation. The number of chemotherapy days was evaluated for the patients that received chemotherapy within the last three months. In addition, the patients that underwent chemotherapy at any time from the onset of febrile neutropenia were noted. The day when the patients became febrile neutropenic, and any invasive attempt were also recorded.

The infection foci of the patients were evaluated as one or more foci. The category of unexplained fever was used for the cases in which no focus was detected.

Multinational Association for Supportive Care in Cancer (MASCC) scores were calculated on the day that the patients met the criteria for febrile neutropenia. The patients who had a fever response with the initial

treatment of febrile neutropenia but whose body temperature increased again at least 48 hours after this response were considered to have secondary fever.

Statistical Analysis

In this study, the Shapiro-Wilk test of normality was used for continuous variables. The Mann-Whitney U test was conducted for the variables that were not normally distributed. Descriptive statistics were presented as median (25%-75%) and mean ± standard deviation values. The chi-square test was performed for categorical variables, and the data were shown as frequency and percentages. The binary logistic regression analysis was conducted to determine the probability of occurrence of the disease according to risk factors. The goodness-of-fit of the model was evaluated according to the Hosmer Lemeshow test. IBM SPSS Statistics v. 20.0 *(SPSS Inc., Chicago, Illi-nois)* was used for statistical calculations. The statistical significance was taken as $p < 0.05$

RESULTS

A total of 174 patients has been included in the analysis and 32 (18.5%) died while 142 (81.5%) did not develop mortality. The comparison of the demographic characteristics and p values of the mortality and non-mortality groups was denoted in Table 1.

The mean age was 63.8 ± 13.1 years in the mortality group and 52.5 ± 16.4 in the non-mortality group, indicating no significant difference. There was also no significant difference in mortality according to gender. The mean fever response time was found to be 5.5 ± 3.9 days in the mortality group ($p = 0.008$). Chronic diseases were similar in the two groups, with no statistically significant difference. In the mortality group, 19.5% of the patients died on the day of hospitalization, with no statistically significant difference compared to the other group. In the same group, the rate of con-fusion was 21.8%, hypotension 31.2%, acute renal failure 37.5%, mucositis 50%, central venous catheter 25%, and urinary catheter 18.7%, and these were statistically significant (Table 2.).

In the mortality group, the median C-reactive protein value was 136.5 mg/L, and the median pro-

Table 1. Comparison of Demographic Characteristics between the Mortality and Non-mortality Groups of Febrile Neutropenia

Demographic characteristic	Mortality group n = 32 (%)	Non-mortality group n = 142 (%)	*P* value
Age (years)**	63.8 ± 13.1	52.5 ± 16.4	**< 0.001**
Gender			
Male	15 (46.8%)	71 (50%)	0.902
Female	17 (53.2%)	71 (50%)	
Fever*	38.4 °C (38.1-38.6 °C)	38.3 °C (38.2-38.6 °C)	0.600
Fever response time (days)**	5.5 ± 3.9	3.3 ± 2.3	**0.008**
Chronic disease			
Diabetes mellitus	8 (25%)	28 (19.7%)	0.505
Hypertension	8 (25%)	38 (26.7%)	0.838
Chronic renal failure	1 (3.1%)	12 (8.4%)	0.301
COPD	3 (9.3%)	5 (3.5%)	0.153
Chronic hepatitis B carrier	2 (6.2%)	9 (28.1%)	0.985
Coronary artery disease	5 (15.6%)	3 (2.1%)	0.153
Chemotherapy during treatment	11 (34.3%)	44 (30.9%)	0.710
Post-chemotherapy days*	11 (4-19)	8 (5-10.2)	0.366
Length of hospitalization (days)*	19.5 (7-26.7)	14 (10-19.2)	0.223

COPD, chronic obstructive pulmonary disease
*median (quartiles), **mean ± standard deviation

Table 2. Comparison of Clinical Characteristics between the Mortality and Non-mortality Groups of Febrile Neutropenia

Clinical characteristic	Mortality group n = 32 (%)	Non-mortality group n = 142 (%)	*P* value
Clouding of consciousness	7 (21.8%)	2 (1.4%)	**< 0.001**
Hypotension	10 (31.2%)	10 (7%)	**< 0.001**
Acute renal failure	12 (37.5%)	6 (4.2%)	**< 0.001**
Total parenteral nutrition	4 (12.5%)	5 (3.5%)	0.061
Mucositis	16 (50%)	40 (28.1%)	**0.029**
Central venous catheter	8 (25%)	11 (7.7%)	**0.010**
Jugular	4 (12.5%)	5 (3.5%)	
Port	4 (12.5%)	3 (2.1%)	
Subclavian	0 (0%)	2 (1.4%)	
Femoral	0 (0%)	1 (0.7%)	
Urinary catheter	6 (18.7%)	2 (1.4%)	**< 0.001**

calcitonin value was 0.72 ng/mL, and this was statistically significant compared to the non-mortality group. Mortality was not related to hematological malignancy type, but 40.6% of the pa-tients that died had an acute myeloid leukemia diagnosis. While the rate of patients with a clinically or microbiologically proven infection diagnosis was 90.6%, the rate of fever of unknown origin was 9.3% in those who developed mortality. İt was statistically significant. Among these diagno-ses, pneumonia and bacteremia were prominent (Table 3.). Mortality was found to be significantly higher among the patients with secondary

fever which is given in Table 4. (59.3%)

In the mortality group, there was no absolute neutrophil count (ANS) elevation (42.3%) even after one week. The rate of those who did not receive G-CSF in the mortality group was %73.7. The rate of patients whose MASCC score resulted as high risk among those who developed mortality was %59.3 and it was statistically significant. While galactomannan positivity was present in 5 patients (%15.6) in mortality group, it was found positive in 6 patients (%54.2) in those without mortality and a statistically significant. In univariate analysis the patients with a clinical or

Table 3. Comparison of Infection Foci between the Mortality and Non-Mortality Groups

Infection foci	Mortality group n = 50	(%)	Non-mortality group n = 112	(%)	*P* value
Urinary system infection	7	14	26	23.2	0.624
Primary bacteremia	13	26	22	19.6	**0.003**
Bacteremia secondary to urinary system infection	5	10	6	5.3	**0.031**
Bacterial pneumonia	9	18	10	8.9	**0.002**
Fungal pneumonia	8	16	8	7.2	**0.003**
Bacterial and fungal pneumonia	2	4	4	3.6	0.305
Soft tissue infection	2	4	9	8	1.000
Catheter infection	2	4	6	5.3	0.641
Anal abscess/infection	2	4	8	7.2	1.000
Other diagnoses	0	0	13	11.6	
Note: Both groups included patients with more than one diagnosis					

Table 4. Relationship between Secondary Febrile Neutropenia Attack and Mortality

Secondary febrile neutropenia attack	Mortality group		Non-mortality group		*P* value
	n = 32	(%)	n = 142	(%)	
Secondary fever	19	59.3	43	30.2	**0.004**
Blood culture growth in secondary fever	8	25	2	1.4	**< 0.001**
Urinary culture growth in secondary fever	4	12.5	3	2.1	0.186

Table 5. Univariate and Multivariate Logistic Regression Analysis Results (number of independent variables in the model = 1)

Clinical and laboratory data	Univariate logistic regression analysis			Multivariate logistic regression analysis		
	OR	OR 95% CI	*P* value	OR	OR 95% CI	*P* value
Age	1.053	1.022-1.084	**0.001**	1.007	0.956-1.062	0.758
C-reactive protein	1.010	1.005-1.015	**< 0.001**	1.002	0.994-1.010	0.571
Procalcitonin	1.048	1.007-1.090	**0.020**			
Secondary fever	3.365	1.526-7.422	**0.003**			
Secondary fever duration	1.089	0.986-1.201	0.091			
MASCC score	0.736	0.650-0.833	**< 0.001**	0.766	0.586-1.001	0.051
Acute renal failure	13.600	4.588-40.313	**< 0.001**	6.897	0.852-55.819	0.070
Clouding of consciousness	19.600	3.848-99.843	**< 0.001**	0.480	0.026-8.846	0.621
Hypotension	6.000	2.239-16.081	**< 0.001**	0.428	0.035-5.287	0.509
Mucositis	2.550	1.165-5.582	**0.019**			
Galactomannan positiveness	6.786	1.831-25.154	**0.004**			
Central venous catheter	3.970	1.447-10.892	**0.007**			
Urinary catheter	16.154	3.090-84.461	**0.001**	13.920	1.305-148.487	**0.029**
Diabetes mellitus	1.357	0.551-3.340	0.501			
Fungal pneumonia	5.583	1.911-16.309	**0.002**			
Bacterial pneumonia	5.165	1.893-14.090	**0.001**	6.760	1.263-36.191	**0.026**
Bacteremia	3.732	1.612-8.638	**0.002**			
Bacteremia secondary to urinary system infection	4.198	1.195-14.748	**0.025**			
Absence of ANS elevation	103.400	12.471-857.305	**< 0.001**	245.697	20.613-2928.594	**< 0.001**
Granulocyte-colony stimulating factor_not applied	3.516	1.174-10.531	**0.025**			
Clinically or microbiologically proven infection	8.160	2.376-28.020	**0.001**	2.516	0.351-18.023	0.358

OR: Odds ratio

CI: Confidence interval

MASCC: The Multinational Association for Supportive Care in Cancer

ANS: Absolute neutrophil count

micro-biological diagnosis had 8.1 times greater mortality rate compared to those without foci. It was also observed that the mortality rate was increased by 3.3 times among the patients with secondary fever. However, the presence of underlying chronic diseases or hematological malignancy did not increase mortality (Table 5.).

When the highly significant risk factors of mortality were further evaluated with the multivariate analysis, it was determined that mortality was increased by 6.7 times by bacterial pneumonia, 13.9 times by urinary catheterization, and 245.6 times by the absence of ANS elevation after one week (Table 5.).

Table 5 shows the distribution of prognostic factors affecting mortality in patients with febrile neutropenia attacks according to the univariate logistic regression analysis and the rates of factors with a highly significant difference ($p \leq 0.001$).

DISCUSSION

Rosa *et al*. concluded that each one-hour delay increased mortality by 18% and emphasized the need to start empirical treatment within 30 minutes. [1] In our study, 174 febrile neutropenia attacks were followed up, and the mortality rate was found to be 18.2%.

In the current study, the mortality and non-mortality groups were compared, and the mean age was found to be higher in the former ($p < 0.001$). In a multicenter study conducted in Korea by Kim *et al*., it was concluded that patients over 50 years of age had a poor prognosis. [3] In the literature, attention has been drawn to the increasing mortality with age, which has been attributed to the ef-fect of decreased immunity.

In a study investigating mortality among patients with hematological malignancies and bloodstream infections, Mario *et al*. reported that approximately 40% of the patients that died had acute myeloid leukemia (AML), 25% had non-Hodgkin lymphoma, and 13.6% had multiple myeloma. [4] In our study, of the patients in the mortality group, 40.6% were diagnosed with AML, 21.8% non-Hodgkin lymphoma, 15.5% myelodysplastic syndrome, 5% acute lymphoblastic leukemia, and 9.4% multiple myeloma.

In our study, we observed no statistically significant difference in comorbidities between the mor-tality and non-mortality groups. This was a favorable aspect of our study since similar initial comorbidities of the patients allowed identifying the main significant factors affecting mortality.

In this study, the median value of fever was found to be 38.4 °C in the mortality group, and there was no significant difference compared to the non-mortality group. Our clinical observations indi-cated that the highest fever peak could not be expected, especially in patients aged ≥ 65 years or those with cardiopulmonary comorbidities due to the deterioration of vital signs and changes in the mental status. It was determined that after these patients that met the fever criteria were treated with antipyretics, their fever was reduced. In a study by Mukoyama *et al*. evaluating the response of febrile neutropenic patients with AML to initial antibiotic therapy after chemotherapy, the median fever response time was calculated as 7 days. [5] In our study, the mean fever response time was 5.5 ± 3.9 days in the mortality group and 3.3 ± 2.3 days in the non-mortality group, and there was a statistically significant difference. We also examined the relationship between chemotherapy and febrile neutropenia and determined that the median duration of post-chemotherapy was 11 days in the mortality group, with no statistically significant difference compared to the non-mortality group.

Horasan *et al*. investigated the mortality factors of febrile neutropenic patients with bacteremia at Mersin University, Turkey and reported the mean length of hospital stay as 27.4 days. [6] In our study, it was observed that the length of hospitalization was higher than the literature data. This was because it was time for the next chemotherapy cycle for 55 patients receiving treatment for febrile neutropenia, and a total of 62 patients developed secondary fever.

In another study from Turkey evaluating prognostic factors in febrile neutropenic patients, Gencer *et al*. reported that the rate of hypotension was 44% in the mortality group. [7] In our study, hypo-tension was observed at a rate of 50% in the mortality group, and it increased mortality by six times. In another study of prognostic factors in febrile neutropenic patients, Tumberello *et al*. ob-served that although a central venous catheter was required in 54% of the patients in the mortality group, there was no statistically significant difference compared to the surviving group. In addition, the rate of acute renal failure was calculated as 29.5% for the mortality group, and that of hypoten-sion was 9%, with statistically significant differences between the two groups. [4] Kanafani *et al*. evaluated febrile neutropenic patients with bacteremia and concluded that the development of cloud-ing of consciousness increased mortality by 21.2 times. [8] In the current study, clouding of con-sciousness, hypotension, and renal failure were found to be associated with mortality at the time of initial

evaluation, and these factors increased mortality by 19.6, six and 13.6 times, respectively.

In a study conducted in Turkey, Demiraslan *et al*. investigated the effect of Stenotrophomonas maltophilia infections on mortality and determined no significant relationship between mucositis and mortality despite the rate of mucositis being 36% among the patients that died. [9] In the current study, the rate of mucositis was found to be 28.6% in the mortality group, and this condition was observed to increase mortality by 2.5 times. In addition, central venous catheter placement in-creased mortality by 3.9 times, while urinary catheter placement increased mortality by 13.9 times.

The skin and mucosa are the first and greatest defense lines of the human body, and the disappear-ance or the weakening of these barriers and defense systems because of invasive procedures are factors that facilitate the entry of microorganisms. In neutropenic patients, both the qualitative and quantitative insufficiency of leukocytes makes bacteremia inevitable. Therefore, every invasive pro-cedure to be performed on neutropenic patients should be well considered by calculating the bene-fit-harm ratio, and foreign bodies should be removed from the body as soon as possible when there is no longer an indication for an invasive intervention. In our sample, only eight patients had a uri-nary catheter at the time of the febrile neutropenia diagnosis, and due to this limited number, we thought it would be controversial to consider urinary catheterization as a risk factor.

Hii *et al*., who evaluated risk factors in 209 patients diagnosed with candidemia in Taiwan, showed that the mortality rate increased by 3.5 times in patients who had received total parenteral nutrition. [10] In contrast, in our study, the rate of total parenteral nutrition as found to be 12.5% in the mor-tality group and 3.5% in the non-mortality group, indicating no statistically significant difference.

When laboratory values are examined, Massaro *et al*. reported that the initial CRP value of the mor-tality group was 132 mg/L, which statistically significantly differed from the survivor group, while the PCT value was 0.77 ng/mL in the mortality group, with no significant difference. [11] We found similar results in our study. The CRP value was 136 mg/L and the PCT value was 0.72 ng/mL in the mortality group, and there was a statistically significant difference between the two groups in relation to both CRP and PCT elevations. However, the lack of an analysis of CRP and PCT val-ues according to infection foci,

localized or systemic infection can be considered as a limitation of our study. In another study, Osmani *et al*. found the mean ANS value to be 127/mm³ in the mor-tality group and reported a statistically significant relationship between ANS and mortality. [12] Our findings contradict those reported in the literature. We observed no statistically significant differ-ence in the median ANS values of the mortality and non-mortality groups (85/mm³ and 100/mm³, respectively).

Similarly, the median number of leukocyte counts did not significantly differ between the two groups. It is possible to explain these results based on the non-homogeneous distribution of labora-tory data. We consider that this result was obtained because the number of patients with an initial ANS value of 500/mm³ and above was relatively higher compared to the literature. High BK counts, especially in patients with chronic myeloid leukemia and chronic lymphocytic leukemia diagnoses can explain the absence of a statistically significant difference in leukocyte.

In a mortality study of febrile neutropenic patients conducted in Turkey, Calik Basaran *et al*. report-ed that the rate of unexplained fever was 34% in the mortality group, and this rate reached 66% among the patients with clinically or microbiologically proven foci. It was observed that mortality was increased by 6.1 times in patients who developed bacteremia. [13] In our study, the rate of clini-cally or microbiologically proven infection foci was found to be 54.2%, this factor increased mor-tality by 8.1 times. Furthermore, we determined that mortality was increased by 3.7 times by bacte-remia, 4.1 times by bacteremia secondary to urinary tract infection, 6.7 times by bacterial pneumo-nia, and 5.5 times by fungal pneumonia. However, urinary tract infection was not significantly re-lated to mortality in our study.

Study Limitations

The limited aspects of our study; small number of patients and their retrospective nature can be counted.

CONCLUSION

The results of the study showed that in febrile neutropenic patients, mortality was increased by 6.7 times by a diagnosis of bacterial pneumonia, 245.6 times by the absence of ANS elevation, and 13.9 times by urinary catheterization. The small number of patients with urinary catheters was ob-served as a disadvantage of our study. It was concluded that in

febrile neutropenic patients, espe-cially if the ANS was not >500 even after more than 1 week, mortality increased 245. It was thought that this issue should be examined with more detailed studies on ANS.

Authors' Contribution

Study Conception: AG, NE,; Study Design: AG, NE, GO, GU,; Supervision: NE, GU, EG,; Ma-terials: AG, EG, GU,; Data Collection and/or Processing: AG, NE,; Statistical Analysis and/or Data Interpretation: AG, NE, GU, EG,; Literature Review: NE, GU, EG,; Manuscript Preparation: AG and Critical Review: NE, GU, EG.

Competing interests

The authors declare that they have no competing interests.

Abbreviations

AML: acute myeloid leukemia
ANS: absolute neutrophil count
CRP: C-reactive protein
FN: Febrile Neutropenia
G – CSF: granulocyte colony stimulating factor
MASCC: Multinational Association for Supportive Care in Cancer
PCT: procalcitonin
SPSS: Statistics Package for Social Sciences

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Importance of Vitamin D in COVID-19 Patients

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ABSTRACT

Objectives: The severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) virus, was identified as the cause of a severe respiratory illness in Wuhan, China three years ago. The COVID-19 infection, which was declared a pandemic in March 2020, caused more than 600 million people to get sick and close to 7 million people to die. Which people have the disease more severely and who have higher mortality are still the subject of research. We investigated whether vitamin D, whose role in immunity has been known for a long time, also affects the prognosis of COVID-19 infection. COVID-19 is currently the leading cause of death worldwide. Vitamin D is an important micronutrient and has been reported to protect against respiratory diseases by improving immunity. In this study, we aimed to reveal whether the 25-hydroxyvitamin D (25 (OH) D) concentration is associated with the risk and severity of COVID-19 by evaluating vitamin D levels in outpatients or hospitalized patients with the diagnosis of COVID-19.

Methods: In the study, vitamin D levels in 124 COVID-19 cases and clinical course and laboratory findings were analyzed retrospectively between March 11-May 31 2020. Statistical analysis was done using IBM SPSS 23. Kolmogorov Smirnov, Man Whitney U, Kruskal Wallis Test, Chi-square, and fisher extract and risk analysis tests were used. Categorical variables were expressed as %. P value < 0.05 was considered significant.

Results: Vitamin 25 (OH) D level in 32 patients (median 10.2) who were given antiviral treatment and needed oxygen. It was found to be significantly lower than the other 92 patients (median 16.25). When patients who needed oxygen treatment during COVID-19 treatment were examined in terms of vitamin D levels; It was observed that patients with 25 (OH) vitamin D level < 10 needed more O2 (OR: 2,833 CI 95% 1,230-6,528, p = 0.013). In patients with 25 (OH) vitamin D < 10, more patients had pulmonary involvement with thorax CT (OR: 2.225 CI 95% 0.999-4.952 p = 0.048) and these patients had more back pain symptoms (OR: 4,765 CI 95% 1,126-20,163 p = 0.022). Patients with 25 (OH) vitamin D <10 had a greater number of decreased senses of smell and taste (OR: 11,857 CI 95% 1,336-105,214 p = 0.006). In addition, 25 (OH) vitamin D levels were positively correlated with aPTT, while it was negatively correlated with neutrophil/monocyte ratio, glucose, ALT, AST, GGT, and LDH.

Conclusions: Our findings suggest a potential relationship between vitamin D concentrations and the prognosis of COVID-19 infection. Our results support the importance of vitamin D levels in the treatment of COVID-19 and the need for vitamin D supplements in treatment.

Keywords: COVID-19, vitamin D, pneumonia

The pandemic coronavirus disease (COVID-19) is currently the leading cause of death worldwide. To date, no curative medication has been found for the definitive treatment of this disease. Future measures, especially vaccines, masks, and social distancing are the most important ways to prevent the social transmission of this disease.

Vitamin D is an important micronutrient and has been reported to protect against respiratory diseases by improving immunity. [1,2]

In this study, we aimed to reveal whether the 25-hydroxyvitamin D (25 (OH) D) concentration is associated with the risk and severity of COVID-19 infection by evaluating vitamin D levels in outpatients or hospitalized patients with the diagnosis of COVID-19.

METHODS

In the study, the test results of 124 cases whose vitamin D levels were measured between March 11, 2020 and May 31, 2020 were analyzed retrospectively. COVID-19 RT-PCR results in nose and throat swab samples, clinical course, and laboratory findings of the patients were retrospectively analyzed. Statistical analysis was done using IBM SPSS 23. Kolmogorov Smirnov, Man Whitney U, Kruskal Wallis Test, Chi-square, and fisher extract and risk analysis tests were used. Categorical variables were expressed as %. P value < 0.05 was considered significant.

RESULTS

RT-PCR test was found positive in 33.9% of 124 patients whose 25(OH) vitamin D levels were checked out of 2800 patients included in the study and whose nose and throat swabs were tested for COVID-19. The 25(OH) vitamin D levels of these patients are shown in Table 1 according to their clinical characteristics. In 32 patients (median 10.2) who were given antiviral drug therapy after lung involvement, 25(OH) vitamin

Table 1. Vitamin D levels according to the clinical characteristics of the patients

		N	%		Median		
RT-PCR	RT-PCR positive	42	33,9	0,452	13,55	4,2	93
	RT-PCR negative	82	66,1		16,05	2,22	97,2
Follow up	In ICU	24	19,4	0,221	12,1	6,3	44,9
	Inpatient	100	80,6		16	2,22	97,2
	Outpatient						
Prognosis	Death	7	5,6	0,673	15,9	6,3	19,8
	Live	117	94,4		14,4	2,22	97,2
Gender	Male	58	46,8	0,896	14	4,2	93
	Female	66	53,2		15,45	2,22	97,2
Vitamin D	< 10	40	32,3				
	> 10	84	67,7				
Vitamin D	< 20	87	70,2				
	> 20	37	29,8				
Vitamin D	< 30	108	87,1				
	> 30	16	12,9				
Antiviral or O2	Take	32	25,8	0,013	10,2	4,2	47,3
	Not taking	92	74,2		16,25	2,22	97,2
Infitration on CT	Positive	66	53,2	0,212	12,9	4,2	97,2
	Negative	17	13,7		16,15	2,22	36,7
	No CT	41	33,1				
	Outpatient	32	25,8				
	Inpatient	92	74,2				

Table 2. Correlation analysis between vitamin D and laboratory values

25 (0H) Vitamin D	R value	*P* value
Neutrophil / monocyte	-0,182	0,058
APTT	0,240	0,029
Glucose	-0,321	0,016
ALT	-0,191	0,045
AST	-0,252	0,008
GGT	-0,261	0,017
LDH	-0,252	0,021

D levels were found to be significantly lower than the other 92 patients (median 16.25).

When patients who need oxygen therapy during COVID-19 treatment are examined in terms of vitamin D level; It was observed that patients with 25 (OH) vitamin D levels < 10 ng/ml had higher oxygen demand and antiviral therapy was started in these patients (OR: 2,833 CI 95% 1.230-6.528, *p* = 0.013). It was observed that patients with 25 (OH) vitamin D < 10 ng/ml had more frequent lung involvement with thorax CT compared to those without (OR: 2.225 CI 95% 0.999-4.952 *p* = 0.048). It was also observed that myalgic symptoms such as low back pain were more common in patients with 25 (OH) vitamin D < 10 ng/ml (OR: 4.765 CI 95% 1.126-20.163 *p* = 0.022). We determined that the symptom of decreased sense of smell and taste also occurred more frequently in patients with 25 (OH) vitamin D < 10 ng/ml (OR: 11,857 CI 95% 1.336-105.214 *p* = 0.006).

In addition, 25 (OH) vitamin D levels were positively correlated with aPTT, while negatively correlated with neutrophil/monocyte ratio, glucose, ALT, AST, GGT, and LDH (Table 2).

When the 25(OH) vitamin D levels of the patients who were followed up in the outpatient, hospitalized or intensive care unit after the diagnosis of COVID-19 were compared, there was no significant difference. Similarly, when the 25(OH) vitamin D levels of the patients whose COVID-19 infection resulted in cure or death were compared, no significant difference was found.

DISCUSSION

When we look at the literature, it is seen that the number of studies examining the relationship between the clinical course of COVID-19 infection and vitamin D levels is increasing day by day.

In a retrospective study, the levels of vitamin D at the time of diagnosis in 212 patients with SARS-CoV-2 infection were examined and it was found that there is a relationship between the prognosis of the disease and vitamin D levels. [3] In our study, we found that patients with low vitamin levels had more severe COVID-19 and needed additional supportive treatments.

In a cohort study of 43 patients, the group was given vitamin D (1000 IU), Mg (150 mg), and vitamin B12 (500 μg) worsened less frequently (*p* = 0.041) than the control group. [4] In a retrospective observational study conducted in Belgium, 186 SARS-CoV-2 PCR positive and 2717 negative patients were examined and it was found that the vitamin D levels of positive cases were lower than the control group (p: 0.0016). [5] We also found in our study that COVID-19 PCR-positive cases had lower 25(OH) vitamin D levels than negative cases. (*p*: 0.452)

In a retrospective cohort study conducted in Indonesia, 780 patients were examined and a correlation was established between low 25(OH) vitamin D levels and mortality due to COVID-19. [6] A similar study was conducted retrospectively on health records in the United States of America and very large patient populations were examined. Exposure to sunlight, vitamin D levels, and COVID-19 infection and mortality were compared over the latitude lived. It has been shown that high vitamin D levels reduce the risk of both COVID-19 infection and related mortality. [7] On the other hand, in a study conducted in the United Kingdom between May and October 2021, Jolliffe and colleagues looked at 25-hydroxyvitamin D concentrations in the blood of 3100 participants, and those < 75 nmol/L were treated with vitamin D3 at a dose of 200IU/day or 800IU/day for 6 months. The control group of 3100 people was not examined or treated. The authors found that none of the vitamin D doses had any effect on the incidence of COVID-19. [8] This trial had several strong aspects: a high prevalence of participants (64.6%) within adequate 25-hydroxyvitamin D levels (< 50 nmol/L), good protocol compliance, and a definitive endpoint with COVID-19 confirmed by polymerase chain reaction.

Although most of the studies in the literature have shown a relationship between vitamin D levels and COVID-19 infection, a small number of studies have not found any relationship between them. In our study, there was no finding that patients with low vitamin D levels had a more fatal course. It was considered that

this was probably due to the low number of deceased patients in our study.

CONCLUSION

Our findings suggest a potential link between vitamin D concentrations and the risk and prognosis of COVID-19 infection. The fact that 25(OH) vitamin D levels are low, especially in patients with involvement in thorax CT and progressing with more severe symptoms, reveals the necessity of vitamin D supplementation. On the other hand; It was evaluated that the lack of significant difference in 25(OH) vitamin D levels in intensive care, hospitalized or outpatient patients due to COVID-19 infection may be due to the rapid replacement of the vitamin when the vitamin level is found to be low or the relatively small number of patients.

It must be admitted that during the pandemic era, which threatens almost the entire society, it is obvious that it is impossible to measure 25(OH) vitamin D levels in all patients who apply to the doctor. At this point; In selected patient groups, it is considered that it would be appropriate to plan treatment according to the result by looking at 25(OH) vitamin D levels or to start 25(OH) vitamin D treatment empirically in patients with certain clinical features. Larger, prospective randomized controlled studies are needed to strengthen this recommendation and confirm the relationship between 25(OH) vitamin D levels and the course and prognosis of COVID-19 infection.

Authors' Contribution

Study Conception: MK, YO,; Supervision: YO, İK,; Desing: MK, YO, İK, ÖÇ,; Data Collection and/or Processing: MK, YO, İK,; Statistical Analysis and/or Data Interpretation: MK, YO, İK, ÖÇ,; Literature Review: MK, YO, İK,; Manuscript Preparation: MK and Critical Review: MK, YO, İK, ÖÇ.

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Evaluation and comparison of depression, anxiety, self-esteem, and social adaptation in hemodialysis and peritoneal dialysis patients

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ABSTRACT

Objectives: The number of end-stage renal failure patients undergoing dialysis is increasing in our country and all over the world. Many patients continues with hemodialysis or peritoneal dialysis lifelong though kidney transplantation is the gold standard renal replacement therapy. The purpose of this study is to compare depression, anxiety, self-esteem and social adaptation in hemodialysis and peritoneal dialysis patients.

Methods: Research consist of 30 hemodialysis and 30 peritoneal dialysis patients who are undergoing dialysis treatment in Uludag University Medical Faculty Hemodialysis and Peritoneal Dialysis Unit. Demographic Data Form, Beck Depression Inventory, Coopersmith Self-Esteem Scale, Social Adaptation Self-evaluation Scale, State and Trait Anxiety Scale were administered to patients.

Conclusion: Self-esteem score of peritoneal dialysis group is significantly high from the hemodialysis group. Peritoneal dialysis group average point was 21.0, hemodialysis group average point was 17.5 on Coopersmith Self-Esteem Scale. There was no significant difference in depression, anxiety and social adaptation scale scores.

Keywords: Depression, Anxiety, Self-Esteem, Hemodialysis, Peritoneal Dialysis

According to the data from the Turkish Society of Nephrology, the prevalence of end-stage renal disease (ESRD) is increasing in our country. [1] In Turkey, the number of patients with ESRD, which was 491 per million population in 2005, has increased approximately twice in numbers in 11 years and reached 933 in 2016, while by 2019 the prevalence and incidence of ESRD were reported as 1007.6 and 150.5 per million population, respectively. [2] Moreover, Turkey was among the top 25 countries with the highest increase rate in ESRD prevalence all over the world between 2009-2018. [3] According to the Turkish Society of 2020 Registry Report, there are 60,558 hemodialysis patients, 3.387 peritoneal dialysis patients, and 19,405 renal transplant patients in Turkey. [4]

Depression is the most frequently reported psychiatric condition in chronic kidney disease (CKD) patients, especially in those with ESRD. [5] The prevalence of depression among patients with CKD can be as high as 100%, depending on the diagnosis criteria and the studied population. [5]

Patients on dialysis have a higher prevalence of depression and a higher risk of hospitalizations due to psychiatric complications compared to their pre-dialysis and post-transplant counterparts. [6] Several

behavioral factors including the burden of self-care, reduced functionality, and the psychology of having a chronic illness and being needed to cope with the disease itself, lead to the development and progression of depression. [7] Nearly 50% of adult CKD patients also have depression and they have 9% increased tendency to be treated with antidepressants. [7] Adequate screening and timely diagnosis of depression throughout the disease are of importance to promote better outcomes in CKD patients. [8]

In this study, we aimed to investigate the psychological status of dialysis patients and compared the patients undergoing peritoneal dialysis and hemodialysis.

METHODS

Study population

Between February 2014 and July 2014, 30 hemodialysis and 30 peritoneal dialysis patients, aged 18 to 65, who was in the routine dialysis program with follow-up in Uludag University Nephrology Department, who had no previous psychological disorders, and were able to read and understand the questions themselves, were included in the study. Demographic data such as age and gender characteristics, duration of dialysis, education level, and level of income were recorded. A total of 5 inventories were used for the evaluation of the psychological status of the patients: Beck Depression Inventory, Coopersmith Self-Esteem Inventory, State-Trait Anxiety Inventory, and Social Adjustment and Self-Evaluation Inventory. This research was approved by Uludag University Faculty of Medicine Medical Research Ethics Committee (February 2014, 2014-3/9).

Psychological Evaluations
Beck Depression Inventory (BDI)

BDI was developed by Beck et al. in 1961 by including the most common symptoms in patients with depression. [9] The validity and reliability of BDI in Turkey have also been reported. [10] BDI consists of 21 items and it's items are evaluated with a score between 0 and 3.

Score distributions for the diagnosis of depression;
- Scores 11-17: Mild depression
- Scores 18-29: Moderate depression
- Scores 30-63: Severe depression

Coopersmith Self-Esteem Inventory

Coopersmith self-esteem inventory is a 57-item scale developed by Coopersmith in 1967 and it is helps with self-esteem scoring. [11] Inventory items are answered in a yes-no format, answers that are accepted as indicators of high self-esteem are given 1 point, and the others are given 0 points. [12] The higher the score obtained from the inventory, the higher the self-esteem of individuals. The study regarding the validity and reliability of the inventory in our country was conducted by Gucluray in 1989. [13]

State-Trait Anxiety Inventory (STAI 1- STAI 2)

The State-Trait Anxiety Inventory was developed by Spielberger and Lushene in 1970. [14] It is two separate tests that were adapted into Turkish literature by Oner in 1977. [15] According to the severity of emotion-behavior in the items of the state anxiety scale (STAI 1) which uses the scoring system as 1) not at all, 2) somewhat, 3) moderately and 4) very much, is very sensitive in assessing sudden changes in emotional reactions. According to the frequency of emotion-behaviors in the items of the trait anxiety scale (STAI 2) which uses the scoring system as 1) seldom, 2) sometimes, 3) often, and 4) almost always, it is very sensitive in measuring the persistence of anxiety (15). High scores indicate high anxiety levels, low scores indicate low anxiety levels.

Social Adaptation Self-Evaluation Scale (SASS)

This scale, which is used to measure social functioning, was developed by Bosc et al. in 1997. [16] Validity and reliability of it were proved by Akkaya et al. in 2008 and were adapted into Turkish literature. [17] The first item of the scale, which consists of 21 items, is filled according to the occupation status, and the remaining 20 questions are answered in the range of 0-3 points. For the person to have normal social functioning, it is necessary to get at least 35 points. If the person gets a score below 25 points, it is considered that there is a problem in social functioning [17].

Statistical analysis

Statistical analyses were conducted using SPSS statistical package program (version 22.0). The distribution of the data was investigated using Shapiro-Wilk normality test. In case the quantitative data is normally distributed independent-samples t-test or else Mann-Whitney U test were used for binary comparison. The categorical data were analyzed by using either Pearson's chi-square, Fisher-Freeman-

Table 1. Socio-Demographic Characteristics of the Patients

	Hemodialysis		Peritoneal dialysis		*p*
	N	%	N	%	
Gender					
Women	11	36.7	15	50	0.434
Men	19	63.3	15	50	
Marital status					
single	5	16.7	7	23.3	0.808
Married	23	76.7	22	73.3	
Divorced	2	6.7	1	3.3	
Educational Status					
Primary school	12	40	12	40	0.533
Secondary school	4	13.3	8	26.7	
Highschool	6	20	6	20	
Undergraduate	7	23.3	4	13.3	
Graduate	1	3.3	0	0	
Total	30	100	100	100	

Halton exact, or Fisher's exact. A p value equal to 0.05 was considered statistically significant.

RESULTS

The demographic characteristics of the patient groups are presented in Table 1. There was no difference between hemodialysis (HD) and peritoneal dialysis (PD) groups in terms of gender, mean age, duration of dialysis, marital status, and educational status. The mean age in HD patients was 54 years, and the mean age in PD patients was 48.5 years. The mean dialysis period in HD patients was 4 years, while it was 6.5 years in PD patients.

There were no significant differences between HD and PD patients with regards to Beck Depression Scale scores (Table 2).

The mean scores of the Coopersmith Self-Esteem Inventory scores significantly higher in PD patients compared to HD patients (*p* = 0.001; Table 3).

There were no significant differences between two patient groups with regards to STAI-1 and STAI-2 scores (Table 4 and 5).

SASS scores were found similar in both patient groups (Table 6).

DISCUSSION

CKD is a progressive chronic disease that requires education on lifestyle changes, nutrition, fluid restriction, and dialysis. [18, 19] However, due to the rapid increase in ESRD incidence and the chances of transplantation is low, the vast majority of these patients living with PD or HD throughout their lives. [20-22] Studies comparing the patient groups on psychiatric morbidity, which is frequently seen in CKD, can provide a valuable idea about which dialysis method can be preferred at first.

Table 2. Comparison of Beck Depression Inventory scores in hemodialysis and peritoneal dialysis patients

Beck Depression Inventory						
	N	Mean	Std. Dev.	Minimum	Maximum	*p*
Hemodialysis	30	11.5	10.005	0	36	0.31
Peritoneal dialysis	30	9.5	8.532	0	40	

Table 3. Comparison of Coopersmith Self-Esteem Inventory scores in hemodialysis and peritoneal dialysis patients

Coopersmith Self-Esteem Inventory						
	N	Mean	Std. Dev.	Minimum	Maximum	*p*
Hemodialysis	30	17.5	4.009	7	23	0.001
Peritoneal dialysis	30	21	3.739	11	25	

Table 4. Comparison of the STAI-1 scores in hemodialysis and peritoneal dialysis patients

STAI-1						
	N	Mean	Std. Dev.	Minimum	Maximum	*p*
Hemodialysis	30	36.5	10.674	20	68	0.314
Peritoneal dialysis	30	34.5	9.401	20	56	

Depression is a common psychiatric disorder in dialysis patients. [23, 24] Studies report that depression makes the person susceptible to infections by suppressing the immune system, therefore, increased mortality rates. [25, 26] Therefore, screening of dialysis patients for depression and referral of risky people to psychiatry clinics are important in clinical follow-up. In our study, the BDI score of PD patients was 2 points lower on average than HD patients, however, this difference was not significant ($p = 0.310$).

In ESRD patients, being dependent on the device used in the treatment and medical team, constant thoughts of death and worries about the future, and deterioration in family relations and work patterns due to their illness adversely affect the patient's self-body image. [27] This can cause the person to lose self-confidence, damage their social relationships, and in the end, stop to look for treatment. [27] In this sense, self-esteem is important for patients receiving dialysis treatment to cope with their disease and adapt to treatment. [27] In our patients, the self-esteem scores of the PD group were significantly higher than the HD group ($p = 0.001$).

Anxiety is a normal part of our daily lives; It is considered normal if it occurs in the presence of danger or threat and if it is suitable for the situation in terms of duration and severity. Three criteria show that anxiety is pathological; violence, duration, and disruption of functionality that affects daily life. Losing a job due to an anxiety disorder is higher than that caused by major depression and has been shown to cause an increase in the frequency of cardiovascular events . [28, 29] In our study, STAI 1 and STAI 2 scores of PD patients were found to be similar to HD patients.

Social functionality is defined as a person's ability to function at work, at home, or in social activities. It also includes the person's ability and competence to maintain a spouse, parent, and social relationship. Many studies have been conducted on the loss of social functionality in depression. [16, 17] In our study,

Table 5. Comparison of the STAI-2 scores in hemodialysis and peritoneal dialysis patients

STAI-2						
	N	Mean	Std. Dev.	Minimum	Maximum	*p*
Hemodialysis	30	43	9.844	27	72	0.088
Peritoneal dialysis	30	40	9.519	22	58	

Table 6. Comparison of SASS scores in hemodialysis and peritoneal dialysis patients

Social Adaptation Self-evaluation Scale						
	N	Mean	Std. Dev.	Minimum	Maximum	*p*
Hemodialysis	30	43.5	8.589	21	59	1
Peritoneal dialysis	30	44	7.85	30	59	

we aimed to investigate the effect of dialysis modality on social functionality by comparing the social adjustment of dialysis patients. The fact that the PD group is less dependent on machinery and healthcare workers for dialysis compared to the HD group may cause these patients to have higher social functionality. In our study, the score of the PD group was found to be higher than the HD group, although it was not statistically significant.

In conclusion, it is observed that psychological problems, especially depression and anxiety, increase in dialysis patients as in all chronic diseases. For this reason, patients' compliance with treatment may decrease and this can affect survival. In our study, we found less depression and anxiety, more self-esteem, and social cohesion in the peritoneal dialysis patients. Decreased addiction of patients, being active in social life, less exposure to interventional procedures, etc. may be effective in this situation. More studies with larger patient groups are required to identify the psychological status of the patients who need continuous healthcare, as it is necessary to diagnose a psychological issue before it is too late for the patient.

CONCLUSION

Authors' Contribution

Study Conception: AG,; Study Design: AG,; Supervision: MY,; Data Collection and/or Processing: AG,; Statistical Analysis and/or Data Interpretation: AG,; Literature Review: AG,; Manuscript Preparation: AG, MY and Critical Review: MY.

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Dietary supplements and Side Effects: Resistant Atrial Fibrillation Jack3d: Resistant Atrial Fibrillation

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ABSTRACT

Dietary supplements, also known as food or nutritional supplements, are intended to compensate for nutrient deficiencies or to maintain the proper nutrient balance in the diet. As dietary supplements are not permitted by law to be marketed as a treatment, prevention, or cure for any disease; only drugs are permitted to make such claims physicians should be aware of the fact that individuals using these supplements could affect their health. A 22-year-old man presented to the emergency department with palpitations and dyspnea of recent onset (>2 hours). His medical history revealed nothing noteworthy. His physical examination revealed tachyarrhythmia. His electrocardiography revealed an AF speed of 130 beats per minute (ECG). In this case, a young man who was using Jack3D and diagnosed with atrial fibrillation has been presented which has been unique.
Despite the fact that natural products in food supplements are more expensive than synthetic ones, the majority of people prefer them. This could be because they believe natural products are more beneficial and safe for their health. As a result, this is a significant public health issue that also poses a financial risk.
Keywords: supplements, side-effects, community health

Dietary supplements also referred to as food or nutritional supplements, are intended to make up for nutrient deficiencies or to keep the right balance of nutrients in the diet. They are the source of nutrients with nutritional or other physiological effects, such as vitamins, minerals, and other substances. They are offered in a form that enables dosing (tablets, capsules, liquids in specified doses).[1] Multicomponent dietary bodybuilding supplements comprise as herbal preparations for the public.[2] Its herbal origin is emphasized while told that has no adverse effect on the promotion.[3] Furthermore, the most frequently reported side effect of supplementary products is ranged from "jaundice and liver failure" to "a seizure with tachycardia and hypertension"

and also "transient ischemia attack".[4] One of these products is Jack3D whichconsists of arginine alpha-ketoglutarate, creatine monohydrate, beta-alanine, caffeine, 1,3-Dimethylamylamine HCl, Schizandrol A, Citric Acid,Natural Flavors, Silicon Dioxide, Acesulfame Potassium, Sucralose, VegetableStearate, Beta Carotene.[5]

When the heart's atria receive errant electrical impulses, which cause rapid and ineffective atrial contraction followed by irregularly irregular ventricular contractions, Atrial fibrillation (AF) happens. In normal sinus rhythm, both the atria and ventricles contract in unison.Atrial fibrillation (AF) in young patients without structural heart disease is rare.[6] Therefore, when the arrhythmia is present in

this population, reversible causes must be identified and resolved. The most frequent causes of atrial fibrillation are hypertension, coronary artery disease, heart valve disease, chronic lung disease, heart failure, cardiomyopathy, congenital heart disease, and pulmonary embolism. Less frequent causes of atrial fibrillation include thyroid disorders and pericarditis. The use of illegal drugs or stimulants, acute alcohol intoxication, excessive caffeine use, electrolyte imbalance, metabolic disorders, infections, or genetic factors are less frequent causes of atrial fibrillation. [7] When acute atrial fibrilation detected in a patients EKG , converting to sinus rytm in 48 hours and cardiac rate control is important for cardiac wellbeing . First and second line therapies are for medical cardiyoversion and rate control. The third line therapies are atrioventricular node ablation , peacemaker and crt . Af treatment has shown in the Fig 1. [12]

This case is noteworthy in that a young man who

developed persistent AF depends on the use of Jack3D, making it an unique example.

CASE

A 22-year-old Caucasian man came to the emergency department complaining of palpitations and dyspnea of abrupt and recent onset (> 2 hours). There was nothing significant in his medical history. His blood pressure was 130/80 mmHg, his pulse was 126/min and arrhythmic, his respiratory rate was 18/min, and his temperature was 36,50C. Tachyarrhythmia was detected in his physical examination. 130 beats/min AF speed was observed in his electrocardiography (ECG). In the emergency department diltiazem and metoprolol applied to the patient , the EKG rythm was still atrial fibrillation . Because of first – line treatment failure. The patient was admitted to the cardiology service for the purpose
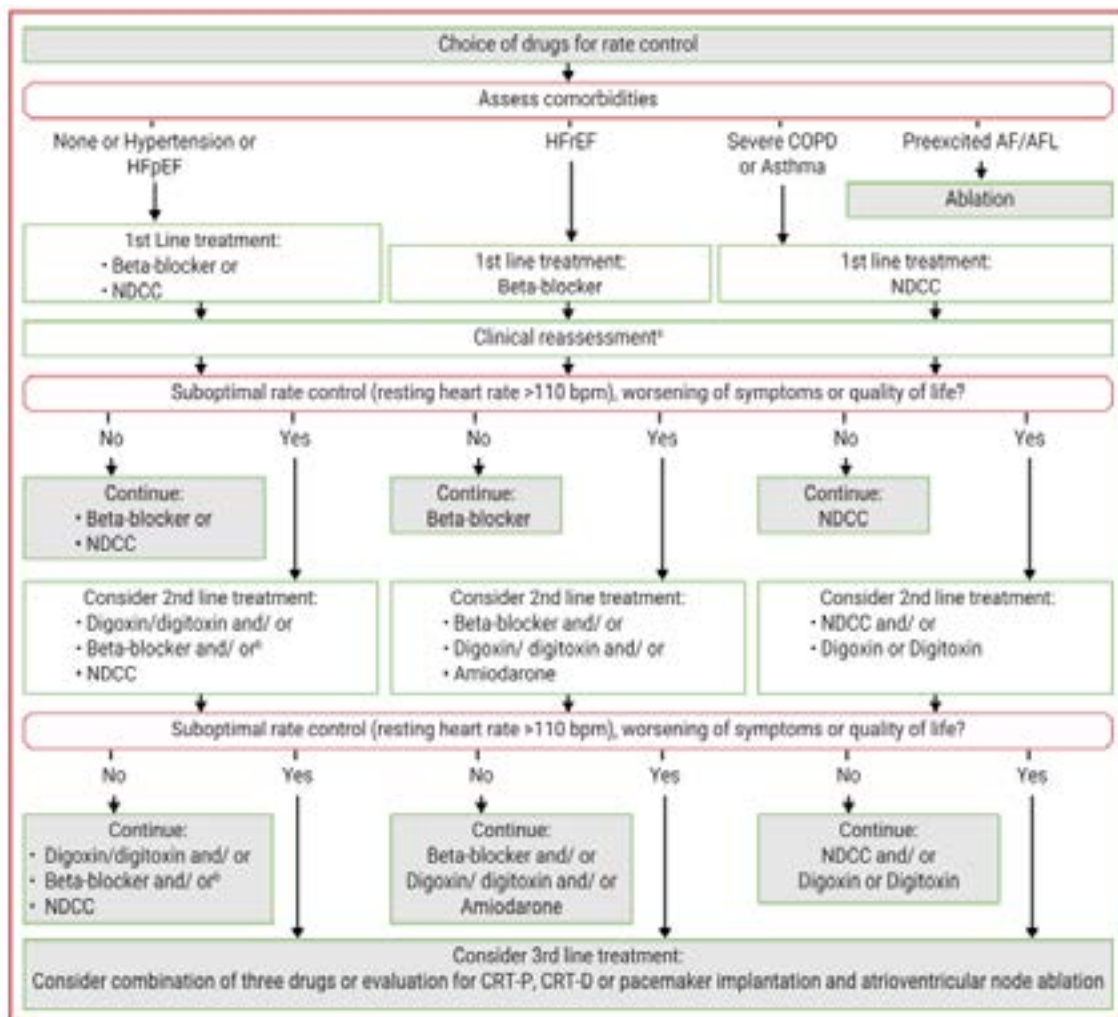

Fig 1. Atrial-Fibrillation-Management

of further evaluation and treatment. No structural cardiac pathology was detected by the transthoracic echocardiography. Amiodarone (Cordarone) infusion (%5 dextrose 100cc, 2 ampuls 1 hour period) was applied and continued for 24 hours period (%5 dextrose 100cc, 8 ampuls). The patient converted to normal sinus rhythm after the second line therapy was started. On direct questioning about herbal products and dietary supplements, he revealed that he took Jak3d which was a bodybuilding supplement.

DISCUSSION

Self-administrationof supplements is causing increasing concern because it can frequently beindiscriminate, and unhealthy, and act as a gateway drug to more dangerous drugsand substances. [8] Zeijon *et al* revealed that *"Protein,DMAA, Cafeine, Creatine, Methasteron, Testosterone, Anabolic steroid, Synephrine, Methylstenbolone, Nandrolone, Citrus aurantium"* were the most reportedsupplements for adverse effects. [3] In Turkey, especially in the Trakya region, *"Glucosamine Chondritin, Biotin (vitamin B7), Coenzyme Q-10, Panax Ginseng, St.John's Wort, Vitamin B12, Vitamin C, Vitamin D3, Multivitamins, Iron, Calcium, Magnesium, Zinc Folic Acid (vitamin B9), Fish Oil (Omega 3, 6, 9 Fatty acids)"* wasreported as most frequently used supplements. [9] Campbell *et al* reported that thereason to use supplements were "Key themes that influenced supplement usewere weight loss, body image, nutrition, training, education, challenges, need,and time." [8] The concept that all ingredientsderived from plants are safe for consumption has led to a recent rise in theuse of supplements. [1] The main purpose of multi-component dietary supplements for bodybuilders is to increase muscle mass. Numerous studies have shown that using the compound creatine and arginine-alfaketoglutarate increases muscle endurance, and that performing multiple Wingate tests shows an improvement in muscle power. However, it is important to not undervalue the risk of fatal side effects in young adults, particularly cardiovascular side effects. [3,5] According to a research which was published in 2021; especially 1,3-dimethylamylamine is the most detected supplement in doping samples. So we can say that 1,3-dimethylamylamine has a very common use as doping in the atletics. [11] İn our case, it's not clear whether JACK3D which have integrients caused

atrial fibrillation (AF). If 1,3-dimethylamylamine supplement is responsible for AF, all athletics who use doping have a high risk for atrial fibrillation. This need further more study.

The market for dietarysupplements is estimated to be worth USD 120 billion, and in recent years, ithas grown by about 6% annually. Asia, North America, and Europe are the primary sales regions. [1] The respondents of the Çoskun's research prefer mostly natural products in food supplements, despite the fact that they cost more than synthetic ones. This could be a result of theirbelief that natural products are more beneficial and secure for their health. 9 So this is an important public health problem that is also an economic threat.

Furthermore, during COVID-19, supplements are used and but for the purpose of preventingor treating COVID-19, there are currently insufficient data to support either recommendations for or against using specific vitamins, minerals, herbs, orother botanical ingredients as dietary supplements. [10]

CONCLUSION

As new challenges means also new options, physicians should be aware of the "history of supplement use" without bias.

Authors' Contribution

Study Conception: ÖG,; Study Design: AKU,; Supervision: ÖG, AKU; Materials: AKU,; Data Collection and/or Processing: ÖG, AKU,; Statistical Analysis and/or Data Interpretation: ÖG, AKU,; Literature Review: ÖG, AKU,; Manuscript Preparation: ÖG, AKU and Critical Review: ÖG, AKU.

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Human metapneumovirus pneumonia during the Sars Cov-2 pandemic

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ABSTRACT

Human metapneumovirus (HMPV) is a virus from the paramyxovirus family identified in 2001. It is the second most common cause of lower respiratory tract infection in children after respiratory syncytial virus. In adults, it is mostly seen in the elderly population, immunosuppressive patients or those with a concomitant chronic disease. Human metapnemovirus can cause various clinical pictures ranging from a simple upper respiratory tract infection to bronchiolitis and asthma attack, from severe pneumonia to encephalitis and acute respiratory distress syndrome. In the case of viral infection in adults, especially during the Covid-19 pandemic, clinical and laboratory findings are similar, so it should be kept in mind in the differential diagnosis. This article is presented to draw attention to the inclusion of HMPV in the differential diagnosis of a 65-year-old female patient who applied to the practice with the complaints of high fever, cough, wheezing and headache during the Covid-19 pandemic. It has become important to detect the causative agent with multiple molecular tests and direct antigen tests in terms of differential diagnosis in respiratory tract infections, which are generally seen in adults during the pandemic. After the viral agent is determined with the diagnosis of the causative agent, the infection can be controlled more easily with the right treatment and the unnecessary use of antibiotics can be prevented.

Keywords: Metapneumovirus, Pneumovirus, COVID-19

Human metapneumovirus (HMPV) is a virus from the paramyxovirus family, identified in 2001. Data show that HMPV has been responsible for respiratory infections worldwide for at least 60 years. Seroprevalence studies have shown that the first infection occurs before the age of 5 years and people are re-infected throughout their lives. [1] In a Cohort study conducted in Israel, HPMV antibodies were detected in 80% of 2-months-old infants, and seropositivity was found in only 30% of 13-months-old infants. [2] This explains that the antibodies show maternal transmission and that the seropositivity decreases as the antibodies passed from the mother over time. In children aged 24 months, HPMV antibodies are positive at a rate of 52%, and almost all children are infected when they reach school age. In adults, it is mostly seen in the elderly population, immunosuppressive patients or those with a concomitant chronic disease. HMPV, which has an incubation period of 3-5 days, is held responsible for a wide spectrum of diseases ranging from upper respiratory tract infections, bronchiolitis, asthma attack, severe pneumonia, encephalitis and acute respiratory distress syndrome. HMPV infection

and COVID-19 are similar in many clinical features, common symptoms and findings include fever, cough, respiratory distress, rhinorrhea, crepitation and rales in respiratory sounds, shortness of breath, pharyngitis, otitis media, and conjunctivitis. [3] Patients with HMPV are found likely to be older women and those with chronic diseases (such as chronic obstructive pulmonary disease and chronic heart failure). Clinical outcomes during COVID-19 pandemic did not show any significant difference between two viruses.

In this article a 65-year-old female patient who applied to practice with complaints of high fever, cough, respiratory distress and headache during the Covid-19 pandemic will be presented. We wanted to emphasize that HMPV can also be as encountered as a factor in patients who have very similar presentation to Covid-19 pneumonia with negative in Covid-19 PCR tests.

CASE

A 65-year-old female patient with complaints of fever, nasal congestion, cough, headache for a week admitted to our clinic. Although oral antibiotic treatment had already been started her complaints did not regress. Vital signs were as follows: axillary body temperature 38.7ºC, respiratory rate 34 / min., oxygen saturation (sO$_2$) 83%, heart rate 115/min. On physical examination, there were widespread rales in both lungs. The laboratory features were as follows: white blood cell count (WBC) 8540/mm^3, Hemogloblin 13.8g/dL, Hematocrit 42.2%, platelet count 186000/mm3, neutrophil count 4020/mm^3, lymphocyte count 3470/mm^3, and C reactive protein (CRP) 32,8 mg/dL, D-Dimer 0.59mg/L, ferritin 492 ng/mL, serum iron

level 86 ug/dl, aspartat aminotransferase 20 U/L, alanin aminotransferase 25,5 U/L, lactate dehhydrogenase 167 IU/L serum albumin level 4,1 g/dl, serum total protein level:7,1 g/dl, serum magnesium level 2,04 mg/dl, serum calcium level 9,98 mg/dl, serum sodium level 144 mmol/L, serum potassium level 5 mmol/L, total cholesterol level 212 mg/dl, low density lipoprotein 108 mg/dl, high density lipoprotein 65 mg/dl, triglyceride 182 mg/dl, serum creatinine level 0,76 mg/dl, blood urea nitrogen 15,5 mg/dl, serum üric acid level 5,11 mg/dl, thyroid stimulan hormon 1,5 uIU/ml, vitamin B12 538,4 pg/ml. On the chest X-ray, there were scattered, multiple, irregularly circumscribed radiopacities that tended to merge with each other in both lung parenchyma, and Thorax CT (computer tomography) was performed thereupon. In Thorax CT, interlobular septal and peribronchovascular interstitial thickenings with patchy ground glass densities-predominantly peripherally located in both lung parenchyma, accompanied by areas of consolidation and tending to merge with each other were detected which were suspicious for atypical viral pneumonia and COVID-19. The patient first performed an outpatient SARS-CoV-2-PCR test. The test came back negative. Meanwhile, the patient was hospitalized due to respiratory distress and persistent fever with the diagnosis of pneumonia. The patient was given 0.5-2 lt/min oxygen support and the SARS-CoV-2-PCR test was performed again. The result came back negative again. Thereupon, HMPV RNA was detected positive by the viral PCR panel taken from nasopharyngeal swab sample. Paracetamol and mucolytic therapy, as well as inhaled and oral corticosteroid therapy were initiated to reduce the patient's symptoms of pain, fever, sputum and cough. The patient's fever and tachypnea were brought under control on the 3rd day

Fig. 1. Chest X Ray

Fig. 2. Thorax CT

of hospitalization. She was discharged home on the 7th day with oral corticosteroid therapy, as her oxygen requirement decreased and her CRP regressed to 6.2 mg/dL.

CONCLUSION

In the Nickbakhsh *et al*. study conducted with 239 samples in the last 4 years, it was observed that HMPV and Covid-19 virus peak overlapped. [4] Since Covid-19 and HPMV virus show similar features both in terms of incidence and clinical findings, their distinction is difficult. Some of the overlapping clinical features are: Cough (COVID-19: 63-69%; HMPV: 82-100%), fever (COVID-19: 80-89%; HMPV: 53-79%), dyspnea (COVID-19: 22-34%; HMPV: 69-98%), expectoration (COVID-19: 28-42%; HMPV: 69%) and some overlapping laboratory indicators are normal leukocyte level and increased CRP levels. [5,6,7,8]

It has been stated that some clinical features may also help distinguish HMPV from COVID-19 infection. Myalgia and fatigue were found to be more common in COVID-19 patients (36-46%), but not in HMPV-infected patients. On the other hand, rhinorrhea (69-85%) and nasal congestion (92-100%) were reported more frequently in HMPV-infected patients than in COVID-19 patients. [9] In our case, there was no myalgia, but she had nasal congestion. Decreased albumin levels (75.8%), lymphopenia (43.1%), elevated D-dimer levels (37.2%) and elevated lactate dehydrogenase levels (28.3-57.0%) have been reported in patients with COVID-19, unlike patients infected with HMPV. [10, 11, 12-15] However, unlike these studies, D-Dimer level was also found to be high in our case.

While female gender, higher age, lower body mass index, suppressed immune system, hematological malignancy or solid organ tumor are factors that increase mortality in HMPV infection; male gender, higher age, high body mass index, leukocytosis, elevated D-Dimer, high LDH levels, hyperglycemia, high-dose corticosteroid usage are found to be high risk factors for mortality in SARS-CoV-2. [16-18] No significant differences were found between thorax CT of HMPV and SARS-COV-2 infection. Ground-glass opacities, consolidations, and bronchial wall thickening are seen in both diseases. [19, 20, 21] However, crazy-paving patterns was not detected in HPMV-associated pneumonias. [22]

In conclusion, the clinical impact of HMPV infection has not changed during the COVID-19 outbreak, with both pathogens being similar in many clinical features. Presence of nasal symptoms, lack of myalgia, elderly patients with low body mass index should bring HMPV to mind.

Despite the negative COVID-19 PCR test results in the SARS-COV2 pandemic, it should not be insisted that the patient has COVID-19 pneumonia and other respiratory disease agents should be quickly screened with very simple antigen tests. This will make a significant contribution to the administration of appropriate antiviral therapy.

Authors' Contribution

Study Conception: ÖK,; Study Design: ÖK, Supervision: ÖO,; Data Collection and/or Processing: SÇ,; Statistical Analysis and/or Data Interpretation: SÇ,; Literature Review: SÇ,; Manuscript Preparation: ÖO and Critical Review: ÖO.

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