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ARAŞTIRMA MAKALESİ

An Investigation of Diabetes Mellitus and Vitamin D Deficiency in Patients Presented to Internal Medicine Outpatient Clinic

Dahiliye Polikliniğine Başvuran Hastalarda Diyabetes Mellitüs ve Vitamin D Eksikliğinin Değerlendirilmesi

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ABSTRACT

Introduction: Vitamin D deficiency plays a role also in the occurrence of autoimmune diseases, including heart disease, cancer, inflammatory bowel diseases, diabetes, and rheumatological diseases. In addition, vitamin B12 deficiency, one of the autoimmune diseases, can also be seen in cases of Vitamin D deficiency. Furthermore, Vitamin D is also associated with insulin secretion and increased insulin sensitivity in target cells, and relevant studies reported Vitamin D deficiency at the initial stage of diabetes mellitus (DM). Accordingly, the present study aimed to investigate the relationship between Vitamin D, DM, Vitamin B12, and ferritin in patients presented to the internal medicine outpatient clinic.

Materials and Methods: The data from adults aged 18 years and over, who presented to the Internal Medicine Outpatient Clinic of the Mersin City Training and Research Hospital between 01 June 2021 and 31 December 2021 were retrospectively investigated.

Results: 476 (95.2%) patients had vitamin D levels below 30 ng/ml, 20 (4.0%) had vitamin B12 levels below 200 pg/ml, and 319 (63.8%) patients had ferritin levels below 20 ng/ml. There was a significant decrease in ferritin in female gender ($p<0.01$), advanced age patients with DM ($p<0.01$), and patients without DM ($p=0.01$).

Conclusion: Vitamin D deficiency plays an important role in the occurrence of many diseases, including DM and Vitamin B12 deficiency. Ferritin, an inflammatory marker, has been shown to be associated with a number of diseases. As a result of the present study, there was a significant decrease in ferritin in advanced age patients with DM, female sex, and patients without DM, and a higher rate of Vitamin D deficiency. Further long-terms studies including post-treatment follow-up periods are required to diagnose the above diseases in an earlier period, prevent complications, and prevent diseases by means of vitamin deficiency treatments.

Keywords: Vitamin D deficiency; Diabetes Mellitus; Ferritin; Vitamin B12

ÖZ

Giriş: D vitamini (vit-D) eksikliği kalp hastalıkları, kanser, inflamatuvar barsak hastalıkları, diyabet, romatolojik hastalıklar gibi otoimmün hastalıkların gelişiminde de rol aldığı tespit edilmiştir. Ayrıca ottoimmün hastalıklardan olan vitamin B12 (vit-B12) eksikliği, vit-D eksikliğinde görülebilmektdir. Bunların yanı sıra vit-D insülin sekresyonun da ve insülinin hedef hücrelerde duyarlılığının artırılmasında da önemli bir role sahip olup, yapılan çalışmalarda diyabetes mellitüsün (DM) başlangıç aşamasında vit-D eksikliği gözlenmiştir. Bu nedenle bu çalışmamızda dahiliye polikliniğine başvuran hastalarda vit-D, DM, vit-B12 ve ferritin arasındaki ilişkiyi değerlendirmeyi hedefledik.

Materyal ve Metod: 18 yaş ve üzeri erişkin, 01 Haziran 2021 ile 31 Aralık 2021 tarihleri arasında Mersin Şehir Eğitim ve Araştırma Hastanesi dahiliye polikliniğine başvuran hastaların verileri retrospektif olarak değerlendirildi.

Bulgular: Hastaların 476 (%95.2)'sinde vitamin D seviyesi 30 ng/ml altında, 20 (%4.0) B12 vitamin seviyesi 200 pg/ml altında, 319 (63.8) ferritin seviyesi 20 ng/ml altında tespit edildi. Kadın cinsiyet ($p<0.01$), ileri yaş ($p<0.01$) DM olanlarda; DM olmayan grupta ferritin düşüklüğü ($p=0.01$) anlamlı tespit edilmiştir.

Sonuç: Vit-D eksikliği DM ve vit-B12 eksikliği gibi bir çok hastalığın oluşumu sürecinde önemli bir rol oynamaktadır. İnflamatuvar bir marker olan ferritinde bir çok hastalık ile ilişkisi gösterilmiştir. Biz bu çalışmamızda DM ile ileri yaş ve kadın cinsiyet, DM olmayanlarda ferritin düşüklüğü anlamlı olup, vit-D eksikliğini yüksek oranda tespit ettik. Bu hastalıkların erken dönemde tespit edilebilmesi, komplikasyonların önlenebilmesi veya vitamin eksikliği tedavileri ile hastalıkların önlemebilmesi için daha uzun dönem , tedavi sonrası takipleri de içeren çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Vitamin D eksikliği; Diyabetes Mellitüs; Ferritin; Vitamin B12

Introduction

Vitamin D is a fat-soluble vitamin produced on the skin exposed to sun rays. It has a key role in the calcium and phosphorus metabolism in our body. (1) Furthermore, the fact that there are Vitamin D receptors on immune system cells, suggests its involvement in the regulation of the immune system. Accordingly, involvement of Vitamin D deficiency has been reported in the occurrence of autoimmune diseases, including heart diseases, cancer, inflammatory bowel diseases, diabetes, and rheumatological diseases.(2,3) In addition, vitamin B12 deficiency, one of the autoimmune diseases, can also be seen in cases of Vitamin D deficiency.(4) Furthermore, Vitamin D is also associated with insulin secretion and increased insulin sensitivity in target cells, and relevant studies reported Vitamin D deficiency at the initial stage of diabetes mellitus (DM).(5,6) Individuals with vitamin D deficiency exhibited a 48 percent reduction in insulin secretion compared to individuals with optimal levels of vitamin D. Thus, indicating that vitamin D stimulates the pancreas to produce insülin.(7)A short-term experimental study suggested that vitamin D supplementation leads to an improvement in pancreatic beta cell functioning and marginally lowers patients' HbA_{1c}.(8)Recent studies on the early diagnosis of DM and its complications suggested that the increase in serum ferritin levels might serve as an inflammatory marker.(9)

Accordingly, the present study aimed to investigate the relationship between Vitamin D, DM, Vitamin B12, and ferritin in patients presented to the internal medicine outpatient clinic.

Materials and Methods

The data from adults aged 18 years and over, who presented to the Internal Medicine Outpatient Clinic of the Mersin City Training and Research Hospital between 01 June 2021 and 31 December 2021 were retrospectively investigated. The patients were screened for age, gender, and comorbid diseases (diabetes mellitus, hypothyroidism).

Vitamin D, Vitamin B12, and Ferritin levels were analyzed (Siemens Healthcare Diagnostics Inc, Laboratory Diagnostics, Advia Centaur XPT, Erlangen, Germany, produced in Ireland). Individuals with vitamin D levels of >30 ng/ml were considered normal, where individuals with vitamin D levels of <30 ng/ml were considered Vitamin D deficient (8); individuals with vitamin B12 levels of <200 pg/ml were considered Vitamin B12 deficient (9), individuals with ferritin levels of <20 ng/ml were considered ferritin deficient, where

individuals with ferritin levels of >220 ng/ml were considered ferritin high. Patients aged over 18 years, who presented to the internal medicine outpatient clinic between June and December 2021 were included in the study. Patients with chronic diseases, including bone diseases and metabolic diseases, and patients, who received Vitamin D treatment in the last 3 months, were not included in the study.

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) Ver. 21.0 (IBM Corp., Armonk, NY, USA) software. The hypothesis of the normal distribution of the variables was tested by the Kolmogorov-Smirnov test. Numerical variables were expressed in median ±SD (standard deviation), where categorical variables were expressed in numbers and percentages. The t test and Mann-Whitney U were used in comparisons between the two groups by numerical variables; where Chi-squared or Fisher exact Chi-squared tests were used for the categorical variables. Required permission for the conduct of the study was obtained from the Non-interventional Clinical Ethics Committee of the Mersin University. (23.02.2022-150)

Results

The mean age of the 500 patients presented to the internal medicine outpatient clinic was 48.4±15.4, where 326 (65.2%) of the patients were female. Diabetes mellitus was the most common comorbid disease in 119 (23.8%) patients. The demographic data of the patients are shown in Table 1.

Table 1. Demographic data

Features	**n: 500**	
	n	(%)
Age mean±SD	48.4±15.4	
Gender		
Male	174	(%34.8)
Female	326	(%65.2)
Comorbidity		
Diabetes Mellitus	119	(%23.8)
Hypothyroidism	31	(%6.2)
Both of them	5	(%1.0)
No	345	(%69.0)
Vitamin D ng/ml median (min-max)	13 (4-87)	
Vitamin B12 pg/ml median (min-max)	350 (125-954)	
Ferritin ng/ml median (min-max)	33 (1-639)	

476 (95.2%) patients had vitamin D levels below 30 ng/ml, 20 (4.0%) had vitamin B12 levels below 200 pg/ml, 319 (63.8%) patients had ferritin levels below 20 ng/ml, and 0 (0%)

patients had ferritin levels above 220 ng/ml. The relationship between vitamin D and age, gender, ferritin, vitamin B12, and diabetes mellitus is provided in Table 2.

Table 2. The relationship between vitamin D and age, gender, ferritin, vitamin B12, diabetes mellitus

Features	**Vitamin D<30ng/ml n:476**		**Vitamin D>30ng/ml n:24**		**P**
Age mean±SD	48.4±15.5		48.6±14.1		0.9
	n	%	n	%	
Female	307	(%61.4)	19	(%3.8)	0.1
Ferritin<20 ng/ml	303	(%60.6)	16	(%3.2)	0.8
Vitamin B12<200 pg/ml	20	(%4.0)	0	(%0)	0.6
Diabetes Mellitus	115	(%23.0)	4	(%0.8)	0.4

There was no significant relationship between vitamin D levels and age, gender, ferritin, vitamin B12, and having diabetes mellitus disease. The relationship between Diabetes Mellitus and age, gender, vitamin D, ferritin, and vitamin B12 is provided in Table 3

Table 3. The relationship between Diabetes Mellitus and age, gender, vitamin D, ferritin, and vitamin B12

Features	**Diabetes Mellitus (+) n:119**		**Diyabetes Mellitus (-) n: 381**		**P**
Age mean±SD	57.9±11.7		45.4±15.4		**<0.01**
	n	%	n	%	
Female	65	(%13.0)	261	(%52.2)	**<0.01**
Vitamin D<30 ng/ml	115	(%23.0)	361	(%72.2)	0.4
Ferritin<20 ng/ml	65	(%13.0)	254	(%50.8)	**0.01**
Vitamin B12<200 pg/ml	4	(%0.8)	16	(%3.2)	0.8

It was significant in female gender ($p<0.01$) and advanced age patients with Diabetes Mellitus ($p<0.01$). In addition, there was significant decrease in ferritin ($p=0.01$) in the non-Diabetic Mellitus group.

Discussion

65.2% of the patients, who participated in the study, were female, where the mean age was 48.4±15.4. In a 2004 study by Akman et al. , 77.7% of the patients presented to the general internal medicine outpatient clinic were female, with a mean age of 50±14.20, where Zülfinaz et al. reported in 2020 that 73.9% of their subjects were female with a mean age of 41.76±15.27 (12,13). The data in our study are indicative of the fact that the rate of women's presentation to

hospital was higher compared to men consistent with the relevant literature.

The prevalence of DM across the world is 7.7%, where according to the TURDEP-1 study the same rate is 7.2% (14,15) in Turkey, and the most common comorbid disease in the present study was DM (23.8%). The present study was designed as a cross-sectional study, and therefore, our rates were high since the assessment was based on the patients, who presented to the outpatient clinic.

In 2020, a meta-analysis by Mahmood et al. reported that 64.6% of healthy people had Vitamin D levels of <30 ng/mL below (16). Pakistani studies reported the vitamin D deficiency ranged from 95.2% to 84.3%, and female individuals account for the 86.4-62.3% (17,18). In the present study, 95.2% of the patients had vitamin D deficiency, where 61.7% were women. A literature review indicated that most of the studies on Vitamin D were conducted in Pakistan. There were higher rates of lower Vitamin D levels associated with women's inadequate exposure to sunlight due to the attire, which covered the entire body, as required by the social norms, lower socioeconomic levels, and sedentary life (19). Given to the similarity of the social norms between Turkey and Pakistan, consistent with the relevant literature the Vitamin D deficiency was more prevalent in women in the present study due to the inadequate exposure to sunlight. It is also important to remember the effect of lower socioeconomic levels and sedentary life on Vitamin D deficiency.

In a study by Jumaa and colleagues, it was revealed that the levels of vitamin D were significantly lower in patients with DMT2 as compared to non-diabetics(20) Sacerdote et al. reviewed the literature extensively to find evidence indicating a correlation between vitamin D deficiency and DMT2. The study reported that current evidence suggests that there is an association between DMT2 and insulin disorders with vitamin D status; however, further studies are warranted(21).

It was reported that there was a relationship between inflammatory markers and DM (22). Besides, certain studies suggested a positive relationship between ferritin, an inflammatory marker, and DM (23). In the present study, there were significantly lower ferritin levels in the non-DM group. A 2021 study in Turkey reported the incidence of iron deficiency anemia as 20.3%, which was considered high (24). In the present study, due to the fact that anemia incidence in Turkey is high, the ferritin decreased to normal levels even it was high, there was no relationship between low ferritin in non-DM individuals.

Neal ES et al. established a female rat model of dietary B_{12} deficiency and identified that four weeks of dietary B_{12} deficiency , promoted glucose intolerance and delayed peak plasma insulin levels following a glucose load, decreased anaplerosis and increased ketogenesis in the liver, depleted hepatic stores of other B vitamins involved in glucose homeostasis, mitochondrial function and one-carbon metabolism and altered liver one-carbon metabolism, leading to changes in methylation capacity and amino acid homeostasis (25).

The limitations of the present study include the fact that it was designed as a cross-sectional study, which included patients, who presented to the outpatient clinic, within a certain time interval, that there was no data with respect to exposure to sunlight, no demographic data, including socioeconomic level, no control group, and lack of long-term post-treatment follow-up. The high number of patients, simultaneous examination of certain parameters, including Vitamin D, DM, Vitamin B12, and ferritin constitute the powerful aspects of the present study.

Conclusion and Recommendations

Vitamin D deficiency plays an important role in the occurrence of many diseases, including DM and Vitamin B12 deficiency. Ferritin, an inflammatory marker, has been shown to be associated with a number of diseases. In the present study, there was a significant decrease in ferritin in advanced age patients with DM, female sex, and patients without DM, and a higher rate of Vitamin D deficiency. Further long-terms studies including post-treatment follow-up periods are required to diagnose the above diseases in an earlier period, prevent complications, and prevent diseases by means of vitamin deficiency treatments.

Conflict of interest:

The authors declared no conflıct of interest

Support Resources

No financial support was received for the study

Ethical Declaration

Required permission for the conduct of the study was obtained from the Non-interventional Clinical Ethics Committee of the Mersin University. (23.02.2022-150)

Authorship Contributions

Concept: DG, SME Design: DG, SME, Supervising: DG, SME, Financing and equipment: DG, SME, Data collection and entry: DG, SME, Analysis and interpretation: DG, SME, Literature search: DG, SME, Writing: DG, SME, Critical review: DG, SME

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