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THE IMPLICATIONS OF PHENYTOIN ON VITAMIN D STATUS: A RETROSPECTIVE STUDY OF OUTPATIENTS AT THE JORDANIAN ROYAL MEDICAL SERVICES

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ABSTRACT

1. Introduction: Vitamin D, essential for bone health and metabolic functioning, is synthesized in the skin under sunlight and further activated by liver and kidney enzymes. Phenytoin, a widely used antiepileptic drug, induces liver enzymes that metabolize vitamin D, potentially leading to reduced levels of this crucial vitamin. Given the importance of maintaining adequate vitamin D levels and the widespread use of phenytoin, particularly among populations with epilepsy, understanding the impact of phenytoin on vitamin D status is of clinical significance. This is especially relevant in regions like Jordan, where despite high sunlight exposure, cultural and dietary factors contribute to prevalent vitamin D deficiency.

2. Objective: This study aims to assess the effects of phenytoin on serum vitamin D levels in a cohort of outpatients at the Jordanian Royal Medical Services during 2021. By examining these effects, the study seeks to determine the necessity for routine monitoring and potential vitamin D supplementation in patients under long-term phenytoin therapy.

3. Methodology: A retrospective cohort study will be conducted involving 66 outpatients (33 males and 33 females) who were prescribed phenytoin and had their vitamin D levels tested in 2021 and vitamin D levels will be categorized as deficient (<20 ng/mL), insufficient (20-30 ng/mL), and sufficient (>30 ng/mL). Data on age and gender will also be extracted from medical records. Descriptive statistics will be used to summarize the demographic and vitamin D data, while independent t-tests will be performed to assess the differences in vitamin D levels between genders. The study primarily focused on identifying trends and significant deviations in vitamin D levels among the phenytoin-treated patients, providing a foundation for potential clinical recommendations regarding the monitoring and management of vitamin D status in this population.

Key Words: Phenytoin therapy, Vitamin D metabolism, Serum vitamin D levels, Bone health, Jordanian Royal Medical Services, Outpatient care, Drug-induced nutrient depletion, Vitamin D deficiency risks, Clinical monitoring, Nutritional management.

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1. INTRODUCTION:

Importance of Vitamin D in Health:

Sometimes called the "sunshine vitamin," vitamin D is essential for many physiological functions, such as controlling cell growth, immune system and neuromuscular function, and reducing inflammation. Most importantly, it is critical for the gut's absorption of calcium, which is necessary to preserve ideal bone health[1]. Lack of vitamin D has been linked to a higher chance of developing a number of bone diseases, including osteoporosis in adults and rickets in children. These conditions are characterized by weakened bone tissue and a greater likelihood for fractures. In addition to its effects on the skeletal system, a lack of vitamin D has been connected to a higher risk of chronic illnesses such diabetes mellitus, cardiovascular disease, and several types of cancer[2,3].

Phenytoin and Vitamin D Metabolism:

Anticonvulsants such as phenytoin are frequently used to treat partial and generalized tonic-clonic seizures. By inhibiting voltage-gated sodium channels, it primarily works by lowering neuron excitability and so averting epileptic discharges[4]. Nonetheless, phenytoin has been recognized to exhibit intricate interplays with many pharmaceuticals and endogenous substances, with its impact on vitamin D metabolism being among the most noteworthy. Hepatic cytochrome P450 enzymes are stimulated by phenytoin and play a role in the breakdown of vitamin D into inactive metabolites. The primary circulating form of vitamin D and a crucial marker of vitamin D nutritional status[5], 25-hydroxyvitamin D, is rapidly degraded as a result of this enzyme activation, which may result in decreased serum levels of the vitamin.

Clinical and Epidemiological Relevance:

Numerous epidemiological studies have demonstrated the prevalence of vitamin D deficiency in a range of populations, highlighting the substantial public health consequences associated with this illness. Despite plenty of sunshine, vitamin D deficiency is surprisingly frequent in Jordan and the wider Middle East[6]. This is due to cultural behaviors including wearing cover-ups, limiting outside activity, and dietary insufficiencies[7]. It is important to comprehend the degree and significance of this interaction because phenytoin may exacerbate this insufficiency, posing extra health concerns for individuals taking this medicine. Because phenytoin is widely used in many different medical settings and is a significant component of treatments for neurological conditions, it is critical to determine whether regular use of this medication calls for strategies for managing vitamin D levels in order to prevent the negative effects of deficiency.

Study Rationale and Objectives:

With that in mind, the purpose of this study is to assess the effect of phenytoin on serum vitamin D levels in a cohort of outpatients treated at Jordan's Royal Medical Services in 2021. By concentrating on this particular population, the study aims to ascertain the prevalence of vitamin D deficiency among phenytoin-treated patients, evaluate the necessity of routinely monitoring and supplementing with vitamin D as part of the comprehensive management of patients on phenytoin therapy, and investigate any potential associations between changes in vitamin D levels caused by phenytoin and demographic factors like age and gender.

This study will add significant information to the body of knowledge and may have an impact on clinical recommendations for the care of phenytoin-using patients, especially in areas where vitamin D insufficiency is already a known public health concern.

2. METHOD:

In this retrospective analysis, the Jordanian Royal Medical Services' 2021 medical records for 66 outpatients—33 men and 33 women—who were prescribed phenytoin were examined. Participants ranged in age from 21 to 89. Data on the patients' demographics (age, gender), phenytoin prescription details, and serum vitamin D levels (ng/mL) was gathered from their electronic health records. The following categories applied to vitamin D levels: insufficiency (20–30 ng/mL), sufficiency (>30 ng/mL), and deficiency (<20 ng/m) (figure 1).

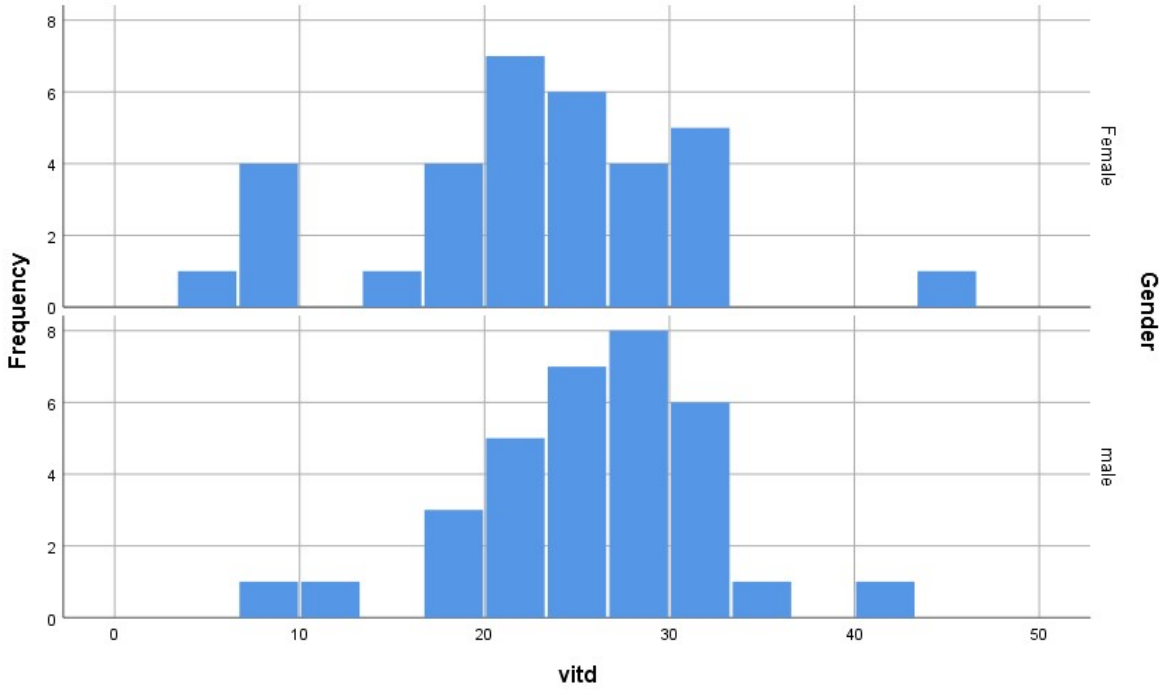

Figure 1: categorization of vitamin D levels among participants

The mean, median, and standard deviation of age and vitamin D levels were calculated, along with other descriptive statistics that summarized clinical and demographic factors. The mean vitamin D levels across genders and age groups were compared using independent t-tests. SPSS software was used for all of the analyses.

In conclusion, the study's methodological approach comprised thorough demographic investigation and statistical testing to investigate how phenytoin affected the levels of vitamin D in a specific outpatient population at the Jordanian Royal Medical Services.

3. RESULTS:

Descriptive and Statistical Analysis: Our results support a decreasing pattern in vitamin D levels, with a significant fraction of the population showing insufficiency or deficiency (Table 1).

Table 1: Categorization of vitamin D levels by gender

Vitamin D Category	Overall (N=66)	Male (n=33)	Female (n=33)
Deficient (<20 ng/mL)	15 (22.73%)	5 (15.15%)	10 (30.30%)
Insufficient (20-30 ng/mL)	37 (56.06%)	20 (60.61%)	17 (51.52%)
Sufficient (>30 ng/mL)	14 (21.21%)	8 (24.24%)	6 (18.18%)

Analysis of Phenytoin and Vitamin D Relationship:

The lack of a noticeable gender difference in vitamin D levels implies that phenytoin's effect on vitamin D metabolism is the same in individuals irrespective of gender male and female. This gender-neutrality suggests that phenytoin's ability to induce enzymes probably outweighs any possible biological differences between males and females with regard to vitamin D metabolism (Table 2).

Table 2: The variation in vitamin D levels by gender

Gender	N	Minimum	Maximum	Mean	Std. Deviation
Male	33	7.63	40.8	22.93	5.962
Female	33	6	43.8	25.67	8.879
Total	66	6	43.8	24.30	7.629

Our results also imply that phenytoin's impact on vitamin D metabolism is constant across age groups, suggesting that phenytoin's ability to induce hepatic cytochrome P450 enzymes is independent of age in terms of vitamin D metabolism (Table 3).

Table 3: Age Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Male	33	21	85	55.85	18.734
Female	33	29	89	60.36	16.880
Total	66	21	89	58.11	17.839

4. DISCUSSION:

Interpretation of Findings: The average vitamin D level in the group of outpatients treated with phenytoin is close to the lower limit of what is deemed insufficient, according to the study's data, indicating a tendency towards decreasing vitamin D levels. This result is consistent with the established pharmacokinetic effects of phenytoin, particularly with regard to its activation of hepatic enzymes involved in the metabolism of vitamin D into inactive forms[8]. The fact that there was no statistically significant variation in vitamin D levels between patients who were male and female as well as between age groups suggests that phenytoin's effect on vitamin D metabolism is not gender or age specific.

These findings have important ramifications because vitamin D is crucial for both bone health and proper metabolic functioning. Particularly in a population when there are other risk factors for bone density loss, low levels of active vitamin D may cause bone demineralization, osteoporosis, and fractures[3]. Furthermore, it is important to pay attention to the wider health effects of low vitamin D levels, including any possible connections to immune system malfunction and chronic illnesses.

It is also interesting that, despite being inadequate, the average vitamin D levels found in our study sample did not fall within the range usually linked to a severe shortage. This could indicate a certain amount of external vitamin D acquisition, either via diet or sun exposure, which could somewhat lessen the effects of phenytoin's enzymatic breakdown. But the variation in levels seen suggests that some people are more negatively impacted than others. This could be due to genetic variations in enzyme induction, variations in phenytoin dosage and treatment duration, or variations in sun exposure and food consumption.

Clinical Implications: The results validate the suggestion that patients on long-term phenytoin therapy should have their vitamin D levels routinely monitored. Early detection of patients with inadequate vitamin D levels enables prompt dietary recommendations, lifestyle adjustments (such as more sun exposure), or pharmaceutical treatment[9]. This preventive strategy is especially crucial in areas such as Jordan, where high baseline rates of vitamin D insufficiency are caused by common cultural practices and lifestyle variables.

Limitations: Several limitations of this study need to be taken into account. Our capacity to adjust for confounding variables and establish causality is limited by the retrospective design and dependence on pre-existing medical information. Furthermore, crucial information was lacking, including the length of phenytoin therapy, patient adherence to prescription schedules, specific measurements of exposure to the sun, and dietary vitamin D consumption. These factors should be taken into

account in future studies since they may have a major impact on serum vitamin D levels.

5. CONCLUSIONS:

Our findings demonstrate a strong association between the prescription of phenytoin medication and lower serum vitamin D levels in outpatients receiving care from Jordan's Royal Medical Services. This association implies that phenytoin may have an effect on vitamin D metabolism, which may be significant enough to call for medical attention from healthcare professionals, especially in settings where vitamin D shortage is already a common problem.

The importance of vitamin D in preserving bone health and general metabolic function makes the implications of our findings more noteworthy. It is commonly known that low levels of vitamin D are linked to a number of harmful health effects, including osteoporosis, an increased risk of fractures, and compromised immune systems, to name a few. Therefore, when prescribing and monitoring phenytoin treatment, clinicians must take these consequences into account because the possibility of phenytoin lowering vitamin D levels could exacerbate these concerns.

We stress the significance of regularly evaluating vitamin D levels in patients on phenytoin therapy in view of these findings. This is particularly important for those who already have problems with bone density, postmenopausal women, the elderly, and any individual who is more susceptible to bone-related health concerns. To lessen the possible detrimental effects of phenytoin on bone health, monitoring should involve routine evaluations of vitamin D level and, if required, the application of vitamin D supplements or other corrective treatments.

Therefore, even while phenytoin is still an important therapeutic choice for treating some medical issues, its usage needs to be carefully balanced with preventative actions to correct any resulting vitamin deficiencies. The increasing amount of information, which includes our study as well, emphasizes the necessity of comprehensive patient care techniques that prioritize maintaining overall nutritional and metabolic health in addition to treating the underlying illness.

Recommendations for Future Research

Prospective cohort designs with comprehensive monitoring of phenytoin dosage, medication duration, food consumption, and lifestyle factors including sun exposure need to be the goal of future research. Furthermore, investigating genetic variables that can influence a person's vulnerability to phenytoin-induced alterations in vitamin D metabolism may offer more profound understanding of how to control these consequences for particular patients. Lastly, interventional studies evaluating the effects of vitamin D supplementation in patients receiving phenytoin may aid in determining the best course of action for managing deficiencies and the hazards they-carry.

In conclusion, phenytoin's effects on vitamin D metabolism should not be disregarded, even though it is still a vital part of managing seizures. Appropriate monitoring and management procedures are necessary to reduce the possible health hazards linked to extended phenytoin use.

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