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**ORIGINAL ARTICLE**

# Detection of Subclinical Cardiac Dysfunction in Healthy Medical Workers with Vitamin D Deficiency

***Elshaimaa Ali M.Elsadek Seaoud[1], Moataz A. Elkot[1] , Seham Mahmoud Eldeeb[2], Shaimaa Wageeh[1]***

[1] *Cardiology Department, Faculty of Medicine, Zagazig University, 44519, Egypt.*

[2] *Public Health and Community Medicine Department, Faculty of Medicine, Zagazig University, 44519, Egypt.*

***Corresponding Author:**
Shaimaa Wageeh,
e.Mail:
shaimaa-mmp@hotmail.com

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**ABSTRACT**

**Background:** Vitamin D is a necessary hormone in many tissues including cardiac myocytes. The autocrine and paracrine regulation of cellular growth differentiation and function in several organs depends on it through preventing the activation of the heart's renin-angiotensin system and natriuretic peptides vitamin D regulates calcium Flux, extracellular matrix turnover and myocardial contractility.

Our study aimed to identify the relationship between vitamin D deficiency and myocardial function (both systolic and diastolic) in medical staff with an adverse history of cardiac disease and normal transthoracic echo Doppler parameters. **Methods:** A comparative cross-sectional study involved 80 doctors, nurses, and technicians working at Zagazig University Hospitals; they were divided into two groups based on 25(OH) D levels: Group A (n=40) had a low vitamin D level of <20 ng/mL & Group B (n=40) had an average vitamin D level (>20 ng/ml). Both groups were subjected to conventional echocardiography and tissue Doppler imaging.

**Results:**The study found significantly higher Left ventricular and right ventricular Tei index in group A compared to group B (P value =0.01 and <0.001), respectively We also found a significantly higher tricuspid deceleration time (DT (t)), tricuspid lateral A' and significantly longer tricuspid interventricular isovolumetric relaxation time (IVRT(T) in group A compared to group B. Finally, a receiver operating characteristic (ROC) c urve was performed which showed that 25(OH) D less than 19.5 was found to have 83% sensitivity and 65% specificity in determining a high RV tei index (>0.55).**Conclusions:** Our study showed that Vitamin D deficiency affects both the systolic and diastolic function of the heart.

K**eywords**: Vitamin D, Cardiac function, Tissue Doppler imaging, TEI index

## INTRODUCTION

Beyond geographic location, numerous factors must be considered when considering vitamin D deficiency. Season, age groups, lifestyle characteristics, Vitamin D supplements, gender, and various other factors can all influence the vitamin D level. However, the prevalence of vitamin D deficiency in the general population appears to be around 30%. This is more common among working communities, with outdoor workers being the least affected [1].

Studies have linked vitamin D synthesis and exposure to sunlight. Shift work is defined as work that takes place outside the standard 9 a.m. to 5 p.m. weekday. It might include evening or night shift work, as well as rotating shifts. Sleep disturbance, cardiovascular issues, gastrointestinal and digestive problems, and increased cancer risk, to name a few, have all been linked to shift work in epidemiological studies [2].

Cardiovascular disease (CVD) is the most common cause of death in the developed world and is forecasted to be the leading cause of death and morbidity in developing countries by 2020 [3]

Vitamin D has receptors in numerous tissues, including cardiac myocytes. It is crucial for the autocrine and paracrine control of cellular activity, development, and differentiation throughout a range of organs..[4] Vitamin D inhibits the activity of the cardiac renin-angiotensin system and natriuretic peptides, controls the turnover of the matrix components, calcium flux, and myocardial contractility, and influences the proliferation and differentiation of cardiomyocytes, which may be the mechanism by which vitamin D exerts its anti-hypertrophic and anti-hypertensive effects and defends against myocardial dysfunction.[5,6]

The dangers of vitamin D insufficiency have been the main topic of discussion in recent years. Given the epidemiological evidence that insufficiency is a serious public health issue, this is justified. However, too much vitamin D can have negative effects, including kidney stones, renal impairment, cancer, and even some CVD symptoms (especially when combined with high calcium intake). [7]

the myocardial wall performance may be systematically analyzed using tissue Doppler imaging (TDI) echocardiogram which also has the potential to shed new light on the pathogenesis of heart disease it is an imaging modality that does not require any bodily contact and directly examines myocardium velocities throughout the cardiac cycle it is feasible to obtain information on cardiac wall motion from an area that may not have enough grey scale information on 2-d echocardiography since it does not depend on the amplitude of the reflected wave [8].

Our study aimed to determine the relationship between serum vitamin D levels and both systolic & diastolic function in a sample of healthy middle-aged doctors, nurses, and technicians.

## METHODS

**Study design and setting**

A comparative cross-sectional study was performed at Zagazig University Hospital between May 2021 and December 2021.

**Ethical standards**

Official permission was obtained by the local Institutional Review Board (Zagazig University, Egypt) NO. (ZU-IRB #10040/30-10-2022). The included participants n the study have been reviewed by the appropriate ethics committee and performed following the ethical standards. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki and has been approved by our institutional review board with a waiver of individual consent.

**Study participants**

A random sample of 80 doctors, nurses, and technicians, whose ages ranged between 20 and 40 years old, were included. Medical workers with diabetes mellitus, hypertension, parathormone dysregulation, and valvular heart disease were excluded.

**The sample size** was calculated based on a previous study [9 ].. In Matter et al. (2016), the RV Tei index was 0.54 ± 0.14 in Vitamin D deficient group versus 0.44 ± 0.17 in the average Vitamin D group. At a confidence level of 95% and power of 80%, the sample size is 80 (40 in each group). The participants were divided into two groups based on 25(OH) D levels:

**Group A:** (n=40) had a low vitamin D level (<20 ng/ml)

**Group B:** (n=40) had an average vitamin D level (≥20 ng/ml)

Complete history taking detailed clinical examinations and laboratory assessments of 25oh d levels were done on all study subjects radioimmunoassay was utilized to determine the 25ohd levels in the serum vitamin D specimen is serum collected using standard sampling tubes containing separating gel, and the serum is separated, and preserved at -20 °C, the specimen is stable for 2 weeks at this temperature. The sample is measured on Cobos e 601 analyser thin 2 hours after reaching room temperature.

Most experts agree that vitamin D deficiency should be defined as hydroxyvitamin D ≤ 20ng/ml vitamin D insufficiency is recognized as 21-29ng/ml [10].

**Echocardiography**

Echocardiographic measurements were done using GE Vivid E9, model GA 091568 (Norway), 5 MHz transducers incorporating color flow, pulsed wave, continuous wave Doppler, and pulsed-wave TDI. Two echo cartographers performed all measurements and were blinded to the patients' 25(OH) D level.

Conventional echo and TDI were both done. Pulsed wave Doppler characteristics were applied to determine the peak E wave velocity, peak A wave velocity, and E/A ratio for the diastolic flow through the mitral and tricuspid valves.

For the left and right ventricles in each person, adequate tissue Doppler imaging data were obtained. Systolic myocardial velocity (S'), both early and late diastolic velocity values, and the ratios between them (E', A', and E'/A', respectively) have been measured in the basal regions of the lateral left ventricular wall, septal wall, and right ventricular free wall for tissue velocity imaging.

The Tei index (myocardial performance index) is a measure that represents the left and right ventricles' systolic and diastolic performances. The Tei index in tissue Doppler images is calculated as the ratio of the total of the isovolumic contraction and relaxation times divided by the ventricular ejection time [7]. throughout the same cardiac cycle, all interval measures were made the electrocardiograms QRS complex and s wave start at different times and this interval is known as the isovolumic contraction time the period between the ending of the s wave and the start of the subsequent cardiac cycle is termed as the isovolumic relaxation time

***Statistical analysis***

Statistical analysis was done using SPSS software version 27 (IBM. IBM SPSS Statistics for Windows, Version 27 [11]. Descriptive statistics were generated for all variables. Shapiro–Wilk test was used to determine the distribution characteristics of variables and variance homogeneity. According to the distribution of continuous data, we used the suitable test of significance. Student's t-test and Mann-Whitney U test were used for continuous variables in two groups analysis. One-way ANOVA (F) and Kruskal Wallis test (KW) were used to analyze continuous variables in more than two groups. Pearson's and spearman's correlation coefficients were used to analyze the linear relation between vitamin D and other continuous variables. Pearson's chi-squared test was used to analyze qualitative variables. Receiver Operating Characteristics (ROC) curve constructed to assess serum vitamin D level as a predictor for abnormal RV Tei index. A cut-off value was chosen.

The level of statistical significance was set at p ≤ 0.05.

## RESULTS

Baseline characteristics of the study population are shown in **Table 1**; the mean age of group A was 32.5 ± 5.0 years, and that of group B was 31.6 ± 5.6 years, with no statistical significant difference between the groups. The percentage of males was statistical significant higher in Group B, 40% compared to 22.5 % in group A. On the contrary percentage of females was statistical significantl higher in group A (77.5% in comparison to 60% in group B). The percentage of people who played regular physical exercise was higher in Group B compared to group A (27.5 % compared to 2.5% respectively). We also found a statistical significant difference between both groups regarding regular vitamin D supplementation; 32.5% of group B compared to 10 % of group A received regular vitamin D supplementation in the last three months.

A comparison between different transthoracic echo and tissue Doppler parameters between both groups is shown in **Table 2**. The left ventricular Tei index was statistical significant higher in group A compared to group B (0.45 ± 0.22 and 0.35 ± 0.13), respectively. Regarding right-sided tissue Doppler indices, tricuspid A' was statistical significant higher in the vitamin D deficient group than in the other group (0.15 ± 0.03 and 0.12 ± 0.02), respectively. Both IVRT of the lateral tricuspid annulus and ejection time were statistical significant higher in group A compared to group B (65.9 ± 15.7 and 57.3 ± 17.6 respectively, (P-value = 0.02) and 287.7 ±27.9 msec compared to 270.3 ± 28.7, (P-value=0.02).RV Tei index was also statistical significant significantly higher in group A (0.41 ± 0.12 compared to 0.29 ± 0.07 in group B, P –value <0.001).

**Table 3** shows a correlation between different tissue Doppler indices and low vitamin D in group A. We found a negative correlation between low vitamin D and both IVRT (t) and RV Tei index (P=0.004 and <0.001, respectively).

**Table 4** and **Figure 1** is a ROC curve constructed to show the sensitivity and specificity of vitamin D to determine RV Tei index>0.55. A vitamin D level of less than 19.5 was found to have 83% sensitivity and 65% specificity in predicting a high RV Tei index (>0.55).

**Table 1:** Socio-demographic and occupational characteristics of the studied groups

| Variables | Group A (n=40) | Group B (n=40) | p-value |
|---|---|---|---|
| Age (years):<br>Mean ± SD | 32.5 ± 5.0 | 31.6 ± 5.6 | 0.4 |

| Variables | Group A (n=40) | Group B (n=40) | p-value |
|---|---|---|---|
| Sex:<br>Male<br>Female | <br>9 (22.5%)<br>31 (77.5%) | <br>16 (40.0%)<br>24 (60.0%) | <br>0.09 |
| Marital status:<br>Married<br>Single<br>Divorced / Widow | <br>25 (62.5%)<br>11 (27.5%)<br>4 (10.0%) | <br>19 (47.5%)<br>16 (40.0%)<br>5 (12.5%) | <br>0.4 |
| Working hours per week:<br>Mean ± SD | <br>25.2 ± 5.7 | <br>27.1 ± 6.2 | <br>0.2 |
| Night shifts:<br>Yes<br>No | <br>17 (42.5%)<br>23 (57.5%) | <br>20 (50.0%)<br>20 (50.0%) | <br>0.5 |
| Smart working (online):<br>Yes<br>No | <br>17 (42.5%)<br>23 (57.5%) | <br>14 (35.0%)<br>26 (65.0%) | <br>0.4 |
| BMI (kg/m$^2$):<br>Mean ± SD | <br>26.0 ± 5.5 | <br>26.8 ± 3.1 | <br>0.4 |
| Regular physical exercise:<br>Yes<br>No | <br>1 (2.5%)<br>39 (97.5%) | <br>11 (27.5%)<br>29 (72.5%) | <br>0.003* |
| Patients receiving vitamin D therapy | 4 (10.0%) | 13 (32.5%) | 0.01* |

* Statistically significant

**Table 2:** Transthoracic and tissue Doppler echocardiographic parameters comparison between both groups

| Variables | Group A | Group B | p-value |
|---|---|---|---|
| Mitral E-wave | 0.81 ± 0.17 | 0.78 ± 0.13 | 0.4 |
| Mitral A | 0.54 ± 0.14 | 0.54 ± 0.09 | 0.9 |
| Mitral E/A | 1.5 ± 0.29 | 1.5 ± 0.24 | 0.3 |
| DT | 135.6 ± 43.0 | 121.9 ± 44.2 | 0.2 |
| Tricuspid E | 0.56 ± 0.13 | 0.58 ± 0.12 | 0.6 |
| Tricuspid A | 0.41 ± 0.09 | 0.44 ± 0.13 | 0.2 |
| DT(t) | 150.8 ± 41.4 | 138.2 ± 34.5 | 0.1 |
| Tricuspid E/A | 1.4 ± 0.27 | 1.4 ± 0.28 | 0.7 |
| Mitral S' | 0.13 ± 0.02 | 0.13 ± 0.02 | 0.6 |
| Mitral E' | 0.18 ± 0.04 | 0.18 ± 0.03 | 0.9 |
| Mitral A' | 0.11 ± 0.03 | 0.11 ± 0.02 | 0.8 |
| Mitral E'/A' | 1.8 ± 0.58 | 1.8 ± 0.57 | 0.9 |
| Mitral E/E' | 4.8 ± 1.8 | 4.4 ± 0.89 | 0.3 |
| Tricuspid E' | 0.17 ± 0.12 | 0.15 ± 0.03 | 0.4 |
| Tricuspid A' | 0.15 ± 0.03 | 0.12 ± 0.02 | 0.03* |
| Tricuspid S' | 0.17 ± 0.14 | 0.16 ± 0.03 | 0.7 |
| Tricuspid E/E' | 3.6 ± 1.0 | 3.8 ± 1.0 | 0.4 |
| LV tei | 0.45 ± 0.22 | 0.35 ± 0.13 | 0.01* |
| RV tei | 0.41 ± 0.12 | 0.29 ± 0.07 | <0.001* |
| A/E (M) | 0.68 ± 0.13 | 0.70 ± 0.09 | 0.4 |
| IVCT (m) | 55.1 ± 13.5 | 52.0 ± 17.1 | 0.5 |

| Variables | Group A | Group B | p-value |
|---|---|---|---|
| IVRT | 76.8 ± 49.7 | 50.4 ± 16.8 | 0.01* |
| ET | 290.5 ± 34.2 | 284.5 ± 25.7 | 0.5 |
| IVCT (t) | 49.1 ± 17.0 | 48.6 ± 16.0 | 0.9 |
| IVRT(t) | 65.9 ± 15.7 | 57.3 ± 17.6 | 0.02* |
| ET(t) | 287.7 ±27.9 | 270.3 ± 28.7 | 0.02* |

* Statistically significant

**Table 3:** Correlation between different tissue doppler indices and low vitamin D levels

| Variables | Group A | |
|---|---|---|
| | r | p-value |
| Mitral S' | 0.08 | 0.6 |
| Mitral E' | 0.13 | 0.4 |
| Mitral A' | 0.11 | 0.5 |
| Mitral E'/A' | -0.08 | 0.6 |
| Mitral E/E' | -0.14 | 0.4 |
| IVCT (m) | -0.20 | 0.3 |
| IVRT (m) | 0.02 | 0.9 |
| ET(m) | -0.25 | 0.2 |
| LV tei | 0.11 | 0.5 |
| IVCT (t) | -0.17 | 0.4 |
| Tricuspid E' | -0.19 | 0.3 |
| Tricuspid A' | 0.06 | 0.7 |
| Tricuspid S' | 0.09 | 0.6 |
| Tricuspid E/E' | 0.07 | 0.7 |
| IVRT(t) | -0.53 | 0.004* |
| ET(t) | 0.03 | 0.9 |
| RV tei | -0.57 | <0.001* |

* Statistically significant

**Table 4 :** Receiver operating curve showing sensitivity and specificity of Vitamin D level to abnormal RV tie index

* Statistically significant

| Variable | Vitamin D cut-off | AUC (95%CI) | Sensitivity | Specificity | P-value |
|---|---|---|---|---|---|
| RV tei >0.55 | <19.5 | 0.78 (0.67–0.89) | 83 % | 65 % | <0.0001* |

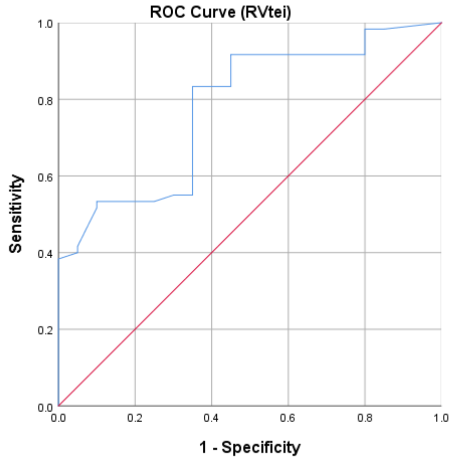


**Figure 1:** ROC curve showing sensitivity and specificity of cut-off value of vitamin D level for Detection of abnormal RV tei index

## DISCUSSION

The effect of vitamin D deficiency on the cardiovascular system is gaining increasing attention; many studies have proved a significant effect of low vitamin D on both systolic and diastolic functions. Our study aimed to determine the effect of low serum vitamin D levels on the systolic & diastolic functions of healthy middle-aged doctors, nurses, and technicians.

Our study showed significantly higher tricuspid deceleration time (DT (t)), tricuspid lateral A', and substantially longer tricuspid interventricular isovolumetric relaxation time (IVRT(t)) in group A compared to group B. The left ventricular tie index was also found to be significantly higher in the same group. Within the vitamin D deficient group, IVRT(t) and RV Tei index were negatively correlated to vitamin D levels. A vitamin D level <19.5 was 83% sensitive and 65 % specific in detecting an RV tei index >0.55.

These results were concordant with Taner Şeker et al. [12]. In their study, Seker and his colleagues found that a lower serum 25-hydroxyvitamin D level was associated with impaired myocardial performance and left ventricle hypertrophy in newly diagnosed hypertensive patients. Seker and his colleagues studied 150 hypertensive patients and divided them into two groups depending on their vitamin D level (vitamin D< 20.00 ng/mL and vitamin D≥ 20.00 ng/mL). when compared to patients with normal vitamin D levels they discovered that vitamin D-deficient individuals had greater IVRT(t) IVCT(t) ET(t) and MPI values in 41 patients with pulmonary arterial hypertension.

Tanaka and his colleagues investigated the correlation between serum 25-hydroxyvitamin d 25oh d levels and the severity of pulmonary arterial hypertension (PAH) a rat model of PAH was fed either ordinary chow or a high vitamin D diet to see whether vitamin D supplementation may stop the development of pulmonary vascular remodeling and RV dysfunction in PAH they came to the conclusion that inadequate vitamin d consumption could accelerate RV dysfunction which would have a significant clinical effect on vitamin D supplementation in PH. Our findings are in line with these results as we found IVRT(t) and RV tei index negatively correlated to vitamin D level [13].

Numerous risk factors for cardiovascular disease have been linked to low levels of vitamin D [14]. Insufficient levels of vitamin D can lead to a rise in the formation of reactive oxygen species and the G protein RhoA, which can block the pathways required for intracellular glucose transfer and lead to the development of insulin resistance.

Furthermore, vitamin D's direct impacts on calcification and smooth muscle proliferation may contribute to how they affect the cardiovascular system [15]. High vitamin D levels were associated with good lipid profile and a lower incidence of metabolic syndrome in the 6784-person Inter99 research [16]. Low l vitamin D have also been linked to cardiovascular disease (CVD) and CVD risk factors like diabetes mellitus (DM), obesity, and hypertriglyceridemia, according to research on NHANES III data from 1988 to 1994 [17].

After multivariable correction, a prospective nested case-control research involving 18,225 US men between 1993 and 1999 found that inadequate vitamin D was linked to a greater risk of myocardial infarction than adequate 25(OH) D. [19].

In a study, Pekkanen et al. evaluated those who had coronary heart disease to see if the (25(OH) D3) concentration would be related to high cardiovascular risk factors and cardiac structure and function. Low vitamin D levels have been linked to cardiac structural abnormalities, heart failure with preserved ejection fraction, and heart failure with reduced ejection fraction, according to their research [20].

Another cross-sectional study involved 640 randomly chosen adults over the age of 45. To discover if the patients with hypovitaminosis D had an association with diastolic dysfunction, the association of vitamin D intake and heart structural and functional abnormalities was examined. They noticed that these people had more instances of diastolic dysfunction [21].

**Limitations of our study**

This is a single-center study with a limited sample size. Larger, multicentre studies are needed. Furthermore, follow-up of patients after treatment to determine whether improvement in TDI parameters and cardiac function is seen.

**Conflict of interest**:

no conflicts of interest.

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