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The Comparison of serum 25-hydroxy Vitamin D in pre-diabetic patients and Individuals with Normal Glucose Tolerance based on Gender among the Patients Referred to Amir Almomenin Hospital, Oncology Clinic during 2012-2014

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Abstract

Introduction: Previous cross-sectional studies have revealed that vitamin D deficiency is associated with prediabetes. Prediabetes increases the risk of type II full diabetes. Considering the significance of diabetes and its high incidence as well as high prevalence of vitamin D deficiency in Iran, more studies need to be carried out in this field to confirm the relationship between prediabetes and vitamin D deficiency. Materials and Methods: It was a case-control study. 208 individuals (55.9%) out of 372 participants were selected as the case group and 164 individuals (44.1%) were selected as the control group based on their fast blood sugar (FBS). The average age of participants was 37.18. Serum 25(OH) D level was compared between the two groups. Findings: No significant difference was observed between serum 25(OH) D of the case group and the control group. Moreover, there was not a significant difference between the two groups regarding their BMIs. Conclusion: No relationship was observed between 25(OH) D and impaired fasting glucose (prediabetes) in individuals with normal FBS. However, it was observed that vitamin D deficiency was quite common among all participants, in such a way that it was observed in 83.6% of all participants. More investigations are recommended to prove the relationship between vitamin D deficiency and prediabetes.

Key words: Diabetes, Vitamin D Deficiency, Prediabetes.

Introduction

Earlier diabetes incidence and its induced morbidity are very high throughout the globe. Presently diabetes is the most prevalent reason for blindness in people aged 20-74 in the U.S.A .In addition, it is the most common reason for kidney failure and non-traumatic amputation of the lower limbs in the U.S. During the last two decades diabetes mellitus outbreak with 30 million cases in 1985 has reached 382 million patients in 2013. Diabetes prevalence in the U.S has been reported 8-16% in various races. The Diabetes International Federation predicts that this disease incidence would reach nearly 592 million cases in 2035 (Kasper et al., 2018; Jalali and Eghbalnejad, 2018). In Iran, diabetes incidence is high as well. In an investigation carried out in Tehran in 2003, raw diabetes and impaired fasting glucose incidences were reported 10.9% and 5% respectively (Hashemipour et al., 2004). In a cross-sectional survey, carried out in Isfahan Oncology and Metabolism Center on 3228 individuals of diabetic families during 2002-2004, metabolic syndrome, type II diabetes, and impaired fasting glucose (IFG) were 35.8%, 10.3%, and 17.3%, respectively (Kelishadi et al., 2014; Holick, 2006). Prediabetes is a condition that makes the person prone to total diabetes. In fact, fast blood sugar is a spectrum, indicating normal blood glucose by levels below 100 mg/dl and diabetes by levels over 126 mg/dl, the interval between these two levels is called prediabetes (or intermediate hyperglycemia based on WHO) (Kasper et al., 2018). Finding out that vitamin D receptors are present in most tissues, and

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conversion of 25(OH)D to 1,25 (OH)D locally occurs in various tissues, has created new insight about the extensive role of vitamin D in the function of various tissues and adverse effects of its deficiency besides calcium deficiency (Stumpf et al., 1979; Holick, 2006). Numerous studies have pointed out uncommon effects of vitamin D, such as adverse effects of its deficiency on cancer occurrence, impaired fasting glucose, type II diabetes, cardiovascular diseases, hypertension, some infectious diseases, and multiple sclerosis. Except for skeletal effects, which are confirmed in interventional studies, for other potential advantages of vitamin D, the present evidence is not certain enough; however, many outcomes obtained from laboratory, animal, clinical, and epidemiologic surveys support these potential advantages (Pittas et al., 2007; Holick, 2006; Modi et al., 2015; Alipour-Parsa et al., 2017). Moreover, studies on both humans and animals have suggested that vitamin D may have a positive effect on insulin secretion and sensitivity either directly or by balancing calcium (Deleskog et al., 2012). It seems that vitamin D supplements decrease blood glucose and blood pressure; however, the relationship between vitamin D and prediabetes in healthy adults is unclear (Gupta et al., 2012). The purpose of this study is to investigate and compare serum vitamin D in people with impaired fasting glucose and people with normal fasting glucose.

According to previous studies, prediabetes and vitamin D deficiency are associated with each other, and if proven, it probably should compensate for this deficit to delay or even prevent prediabetes conversion to total diabetes (Gupta et al., 2011; Gupta et al., 2012; Liu et al., 2011; Barengolts, 2010).

This is important because diabetes has a high morbidity and in addition to problems and disabilities patients face, it imposes heavy costs on health and medical system of the country (Harris et al., 2012). Regarding the high incidence of diabetes and its annual increase in our country and also considering the high incidence of vitamin D deficiency, which is seen in various regions of Iran in both genders (in a survey carried out by Dr. Larijani, et al., on 53299 participants in five cities of Iran with varying latitude and longitude, medium or severe vitamin D deficiency was reported to be 47.85% and 34.75% in women and men respectively) (Sanaei et al., 2017), it seems that studies related to vitamin D deficiency and diabetes incidence in people with prediabetes should be extended so that diabetes incidence can be decreased because compensating for vitamin D deficiency is quite simple, economical, and available. Moreover, despite our research through domestic websites (such as www.sid.ir), there has not been any surveys considering the relationship between vitamin D deficiencies and prediabetes so far; therefore, this issue needs to be investigated.

Method and statistical analysis

This is a cross-sectional epidemiologic descriptive study based on hospital and clinical information, obtained from the patients referred to Amir Almomenin Hospital, Oncology Clinic during 2012-2014. Epidemiologic factors of people, including personal characteristics and clinical symptoms, were precisely extracted using information in patients' files, which were previously inserted by their physicians. Serum 25-hydroxy vitamin D was measured by Euroimmun kit and ELISA method that could measure 4-100 ng/ml range. The lab personnel was unaware of the survey. All patients' informed consent was obtained after providing them with a complete explanation of the title and objectives of the project and ensuring data confidentiality. After completing information and including them in data-collection form, data were analyzed using SPSS version 24 by a statistical engineer.

Results

372 people participated in the current survey among which 315 were female (84.7%) and 57 (15.3%) were male. According to the fast blood sugar level of all subjects whose information were complete, 208 individuals were selected as the case group and 164 were chosen as the control group. The average age of participants was 37.18 (standard deviation: 14.8) and the age range of participants was 8-88. The average body mass index (BMI) was 28.95 among all participants. BMI averages were 28.18 and 29.47 in control group and case group, respectively. The average and median of serum vitamin D among all participants were 18.3 and 13.1, respectively. In order to compare serum vitamin D in case and control subjects, participants were categorized into 4 groups based on their serum vitamin D levels (severe deficiency, medium deficiency, slight deficiency, and normal). The results are presented in Table 1. It should be mentioned that there was not a significant difference among the groups. Moreover, in another analysis of the two control and case groups, subjects with severe, medium, and slight serum vitamin D deficiency were compared with individuals with normal levels of serum vitamin D. The result showed that in the case group 81.2% and in the control group 86.6% of the participants had a serum vitamin D level lower than normal, diagram 5 illustrates the outcomes. In this analysis, no significant difference was observed among groups. BMI was compared between the two groups; in the case group 76.8% of individuals had a BMI over 25 and 23.2% had a BMI lower than 25.

Comparing serum vitamin D in severe, medium, and slight deficiency, as well as normal subgroups was not significantly different. BMI was compared between individuals in case and control groups in subcategories of obese, overweight, normal, and thin which showed no significant difference. Another analysis was also carried out in which the average serum vitamin D levels of the control and case groups were compared within the same season and revealed no significant difference as well. Vitamin D deficiency incidence among all participants including cases and controls was investigated and it was revealed that 83.4% had vitamin D deficiency and 16.4% had normal serum vitamin D level.

Discussion and Conclusion

The results of the present study were obtained based on the files of patients referred to Amir Almomenin Hospital, Oncology clinic during 2012-214.

According to the statistical results, serum vitamin D levels among cases (individuals with impaired fasting sugar) and controls (individuals with normal serum fast glucose) were not significantly different. In a cross-sectional study, done in 2014 in India on 606 participants, vitamin D deficiency was measured in the ranges of fast plasma sugar, impaired fasting glucose, and type II diabetes and found no significant difference among the three groups regarding vitamin D deficiency; however, vitamin D deficiency was seen among 85% of participants (Modi et al., 2015). This was in accordance with our survey. The participants were chosen in the range of 35-56 years old without diagnosed type II diabetes.

Participants' serum 25-hydroxy vitamin D was measured and Oral Glucose Tolerance Test was performed. Subjects who had prediabetes or type II diabetes during 8-10 follow-ups were chosen as cases. At the beginning and end of the study they were matched with controls with normal glucose tolerance (NGT) who were homogenous regarding their age and gender (No. = 980 females and 1398 males). Results: Men, but not women, who were at the highest level of serum 25-hydroxy vitamin D quartile, showed a decreased risk for type II diabetes. This reduction was observed for individuals who firstly had prediabetes, but not the ones with normal glucose tolerance (NGT). In both genders, proceeding from prediabetes to type II diabetes decreased 25% for each 10 nmol/L of 25-hydroxy vitamin D.

High serum level of 25-hydroxy vitamin D predicts a reduced risk for type II diabetes in the patients with prediabetes (Deleskog et al., 2012). These results are not in accordance with ours. As observed in previous studies, there is a controversy over the relationship between serum vitamin D level and prediabetes and varying results were obtained in different studies (de las Heras et al., 2013). In our survey, there was not a significant relationship observed in serum vitamin D and vitamin D deficiency with prediabetes. However, it was observed that 83.4% of all participants suffer from vitamin D deficiency to some extent (serum levels lower than 30 ng/ml) which indicates a high incidence of vitamin D deficiency among all participants. Anyhow because of the selection method of participants, the results may not be generalizable to the whole community. BMI was compared among individuals of case and control groups in obese, overweight, normal, and thin sub-categories which was not significantly different.

Limitations

There were some limitations in this study which may have affected the outcomes:

- The number of participants and the unequal number of cases and controls.
- Background diseases: The participants were chosen among individuals referred to Oncology Clinic and they had disorders such as thyroid malfunction.
- Some information depended on medical history: One of the indices to exclude the survey was taking vitamin D or calcium supplements within the last three months which was merely based on the patients' history.
- Considering global as well as national statistics of vitamin D deficiency, this contradiction is quite evident that vitamin D deficiency incidence is much higher in Iran than in American countries (in the study by Larijani, et al., severe or medium vitamin D deficiency was reported to be 47.85% and 34.75% among women and men, respectively). This huge level of vitamin D deficiency in our country could have led to the insignificant difference between case and control groups regarding vitamin D levels.

Suggestions

As outlined earlier, various studies results about the relationship between serum vitamin D and prediabetes are contradictory. With regard to the significance and incidence of diabetes complications and morbidity, more extensive studies with fewer limitations and errors are needed to find out if vitamin D deficiency is related to prediabetes or not; and if confirmed, can we prevent or procrastinate prediabetes proceeding to diabetes by prescribing vitamin D supplements or not.

Disclosure of interest: The authors report no conflicts of interest.

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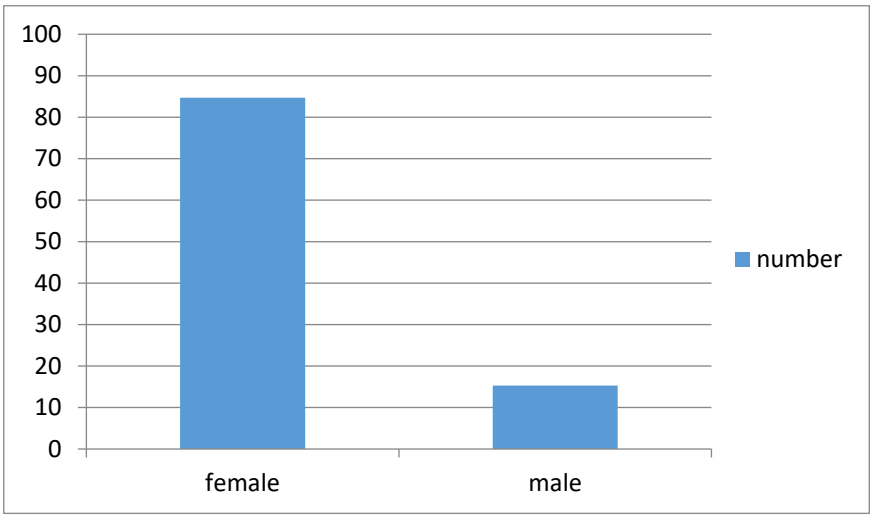

Diagram 1. Frequency of participants based on gender

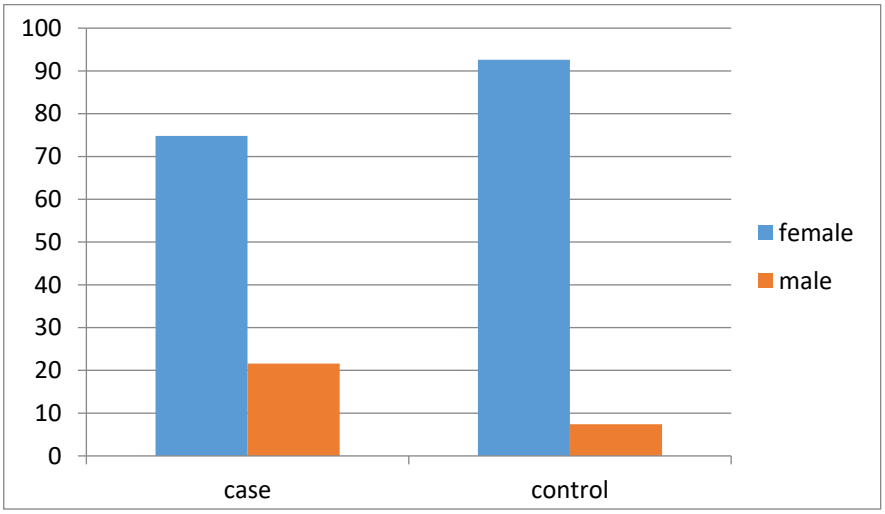

Diagram 2. Frequency of participants' gender based on case and control groups

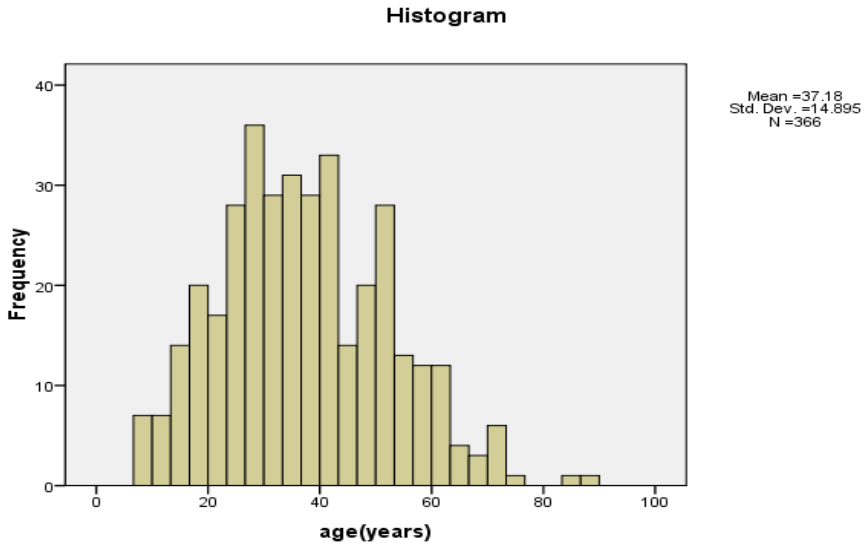

Diagram 3. Age frequency of participants

Table 1. Vitamin D deficiency percentage in 4 sub-groups among cases and controls

	Sever deficiency (%)	Moderate deficiency (%)	Mild deficiency (%)	Normal (%)
case	31/7	32/7	16/8	18/8
control	38/4	33/5	14/6	13/4

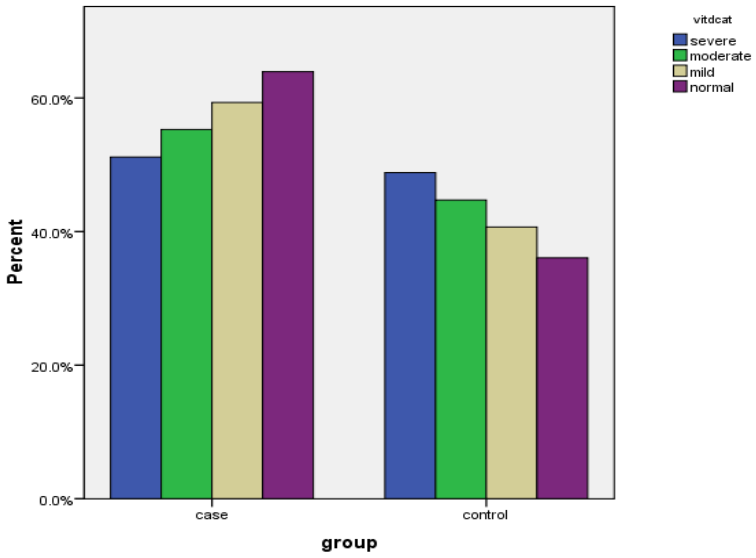

Diagram 4. Serum vitamin D deficiency percentage in 4 sub-groups among cases and controls

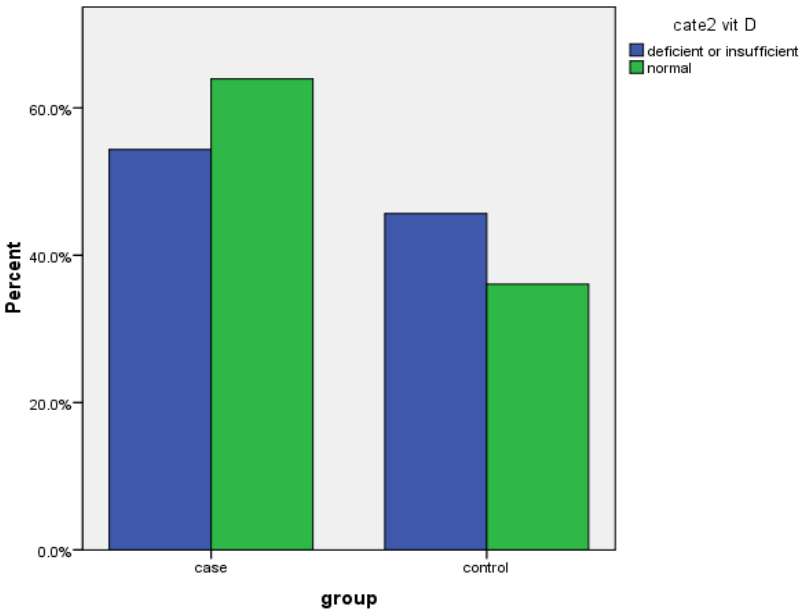

Diagram 5. Comparison of serum vitamin D in two sub-groups of case and control

Table 2. Comparison of mean and median of serum vitamin D and the average of body mass index (BMI) among cases and controls

	mean 25(OH)D ng/ml	**mean 25(OH)D ng/ml**	**mean BMI**
case	14	18.49	29.47
control	12.7	17.87	28.18

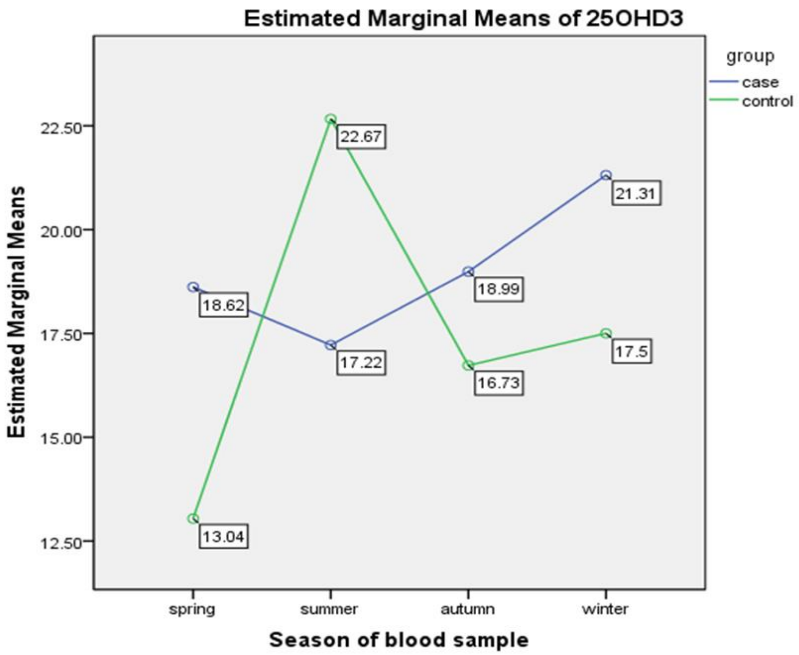

Diagram 6. Comparison of serum vitamin D based on blood sampling season in cases and controls

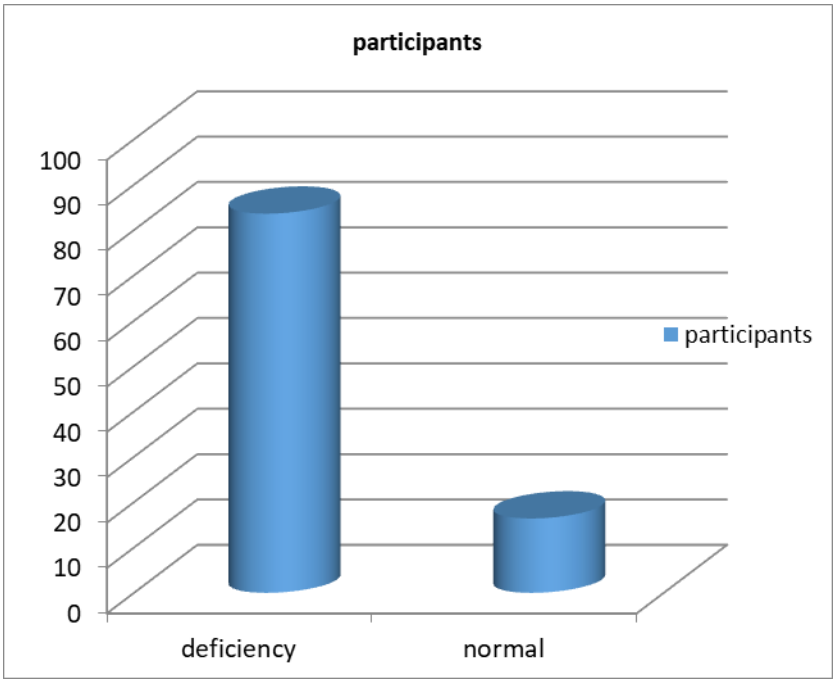

Diagram 7. Frequency of vitamin D normal levels and its deficiency among whole participants (372 individuals)