A COMPARISON OF SERUM LEVELS OF 25-HYDROXY VITAMIN D IN PREGNANT WOMEN AT RISK FOR GESTATIONAL DIABETES MELLITUS AND WOMEN WITHOUT RISK FACTORS

Lobat Jafarzadeh1, Akram Motamedi2, Masoud Behradmanesh3, Raziyeh Hashemi4

1Department of Obstetrics and Gynecology, Shahrekord University of Medical Science, Shahrekord, Iran
2Faculty of medicine, Shahrekord University of Medical Science, Shahrekord, Iran
3Shahrekord University of Medical Science, Shahrekord, Iran
4School of medicine, Baqiyatallah University of Medical Sciences, Tehran, Iran

Corresponding author: Lobat Jafarzadeh , Associate professor, Department of Obstetrics and Gynecology, Shahrekord University of Medical Science, Shahrekord, Iran. Tel: 03832252782, Email: lobatjafarzadeh@gmail.com

ABSTRACT

Background: During pregnancy, Low serum 25-hydroxyvitamin-D [25(OH)D] concentration is even more critical. This deficiency leads to higher incidences of preeclampsia, gestational diabetes, preterm birth, bacterial vaginosis, and also affects the health of the infants. The aim of this study was to evaluate the relationships between serum levels of 25-hydroxyvitamin D (25(OH)D) and gestational diabetes mellitus (GDM) and differences in high-risk pregnant women and women without risk factors for GDM.

Methods: This cross sectional study including 155 pregnant women, who are still in the first trimester of pregnancy (less than 12 weeks gestation), were randomized to two groups of high and low risk for GDM. For these people, once at the gestational age less than 12 times a week and once at 24 to 28 weeks of pregnancy, tests of FBS / BS / HbA1C / 25OHD / insulin / Ca / Albumin was requested. Besides, the OGTT test was performed with 75 g glucose at 24 and 28 weeks of pregnancy to diagnose GDM.

Results: Serum levels of 25(OH)D in the second trimester of pregnancy ng / ml (24.1 ± 39.5) was significantly lower than that of the first trimester ng / ml (25.9 ± 45.6) (p <0.001). But serum 25(OH)D levels in the first and second trimester of pregnancy was significantly different in women at high risk for GDM than women who had no risk factors (p =0.584 and p =0.99). Serum levels of 25(OH)D has an inverse and significant relationship with HbA1C at the beginning of pregnancy (p<0.001). In addition, a significant and inverse relationship was shown between serum levels of 25(OH)D in the second trimester with insulin (p=0.047) and blood sugar 2 hours after ingestion of 75 g glucose (p=0.045) at 24-28 weeks of gestation.

Conclusion: Regarding to the relationship between serum levels of 25(OH)D and blood sugar and insulin at the second trimester of pregnancy, it is recommended for pregnant women to take vitamin D supplementation.

Key words: gestational diabetes mellitus(GDM), 25-hydroxyvitamin D, vitamin D, pregnancy.

1. INTRODUCTION

Gestational diabetes mellitus (GDM) is considered as glucose intolerance with onset or first recognition during pregnancy (1). Prevalence of GDM during pregnancy ranges from 1 to 14 % of all pregnancies depending on the population under study and the diagnostic tests applied (2-4). The prevalence of this type of deficiency is 4.7 % among Iranian pregnant women (5). GDM is associated with increase in risks of maternal and neonatal gestational complicacy and delivery problems, including preeclampsia, preterm labor, cesarean delivery, fetal macrosomia and neonatal hypoglycaemia (6, 7). Those issues trigger GDM become an essential topic for investigation (1) that increases concern in vitamin deficiency as a potential cause (8). Although epidemiologic studies have shown a relatively consistent connection between vitamin D deficiency and a higher risk of type 2 diabetes mellitus (9, 10) and although obesity is associated mainly with both GDM (11,12)and vitamin D deficiency(13-15), it remains dubious whether vitamin D level risks a mother to experience GDM or not. Vitamin D is a prohormone that can be gained from both dietary factors and sunlight exposure (16). The prevalence of 25(OH)-vitamin D deficiency and insufficiency is increasing in Western societies and is particularly common in women of reproductive age and during and after pregnancy (17, 18). Vitamin D deficiency during pregnancy has
been connected to maternal osteomalacia, GDM, preeclampsia, small birth size, respiratory diseases, impaired fetal growth and bone development later in childhood (19-21), and more recently adequate vitamin D level has been linked to embryonic neuro-development (22,23). Epidemiological data have shown that pregnant women with GDM were probably being vitamin D deficient (24). A few studies support relationship between low 25-hydroxyvitamin D (25(OH)D) levels and an increased risk of GDM (25-28), but a recent prospective study did not find any evidence of an association between first-trimester 25(OH) D levels and the further development of GDM (29). Due to previously found differences in vitamin D status in pregnant women, and because pregnancy is a vulnerable period for both the woman and the growing fetus, the aim of this study was to compare of serum levels of 25-hydroxyvitamin D in pregnant women at risk for GDM and women without risk factors.

2. PATIENTS AND METHODS

This cross-sectional study was carried out on 155 pregnant women, who do not yet finished the first trimester of pregnancy (less than 12 weeks gestation). They were selected among 400 pregnant women with gestational age less than 12 weeks during the 5 month, who referred to Shahrekord prenatal care clinics affiliated to Shahrekord University of Medical Sciences, Iran. The design of study was approved by the Ethics Committee of Shahrekord University of Medical Science, Iran. Consent forms were filled in by participants of this study. All the participants have the inclusion criteria in this study. All of them were clinically and thoroughly examined and their medical and health history were completely collected and recorded. The inclusion criteria in this study were: complete and full consent, no intake of calcium supplementation and vitamin D during the past 6 month, the absence of any history of chronic liver disease, renal, endocrine, heart and respiratory disease based on examination and record history, no diagnosed diabetes type 1 and 2, no medication intake medication influence on metabolism, vitamin D homeostasis during the past 6 months and not having previous history of GDM. Exclusion criteria included: lack of consent to continue the follow-up, lack of referring for the next follow-ups, lack of consent to OGTT in the first trimester, emergence of any chronic liver, renal, endocrine, cardiovascular and respiratory disease during pregnancy, emergence of any adverse obstetrical events during pregnancy, forced consumption of drugs influencing metabolism and hemostasis calcium and vitamin D during pregnancy and, definitive diagnosis of diabetes at the beginning of the study based on the experiments done. Method of Sampling was simple sampling. Pregnant women were randomized to two groups of high and low risk based on the existence of at least one of the following criteria: "BMI≥35, history of GDM, birth weight of more 4 kg, any evidence of an association between first-trimester 25(OH)D levels and the number of pregnancies (p = 0.49). As shown in Table 1., there were a significant relationship between serum levels of 25(OH)D and the number of pregnancies (p = 0.49). T-test showed no association between serum levels of 25(OH)D (p = 0.01) with the place of residence. The t-test showed no significant association between serum levels of 25(OH)D and the number of pregnancy (p = 0.49). The results of metabolic parameters in the first and second trimester of pregnancy in patients are summarized in Table 2. Defining the risk factors for GDM (based on the Standard of Medical Care in Diabetes-2012, American Diabetes Association (31)), 27 of 155 patients (17.4 %) were diagnosed with high risk based on the existence of at least one of the following criteria: "BMI≥35, history of GDM, birth weight of more 4 kg, and positive family history for type 2 diabetes. Average level of serum of 25(OH)D for 64 of the cases who were referred in the
second trimester was 32.11 ± 53.9 (ng / ml) at the beginning of the study and was 24.1 ± 39.5 (ng / ml) in the second trimester. Paired t-test showed a significant decrease in the levels of serum of 25(OH)D in the second trimester compared to the first trimester (p <0.001). There was no significant difference for levels of serum of 25(OH)D at the beginning and end of the study in the high risk group comparing the low-risk group (Table 3).

The relationship between serum levels of 25(OH)D and metabolic factors in the first and the second trimester based on the Pearson correlation coefficient is shown in Table 4. There was a direct and significant correlation between serum levels of 25(OH)D in early pregnancy and HbA1C level in the first trimester of pregnancy and there is a direct and significant correlation between serum levels of 25(OH)D in early pregnancy and insulin level, the level of insulin secretion will be reduced as well and this cause increase in the blood sugar. It was shown that there was significant inverse correlation between serum levels of 25(OH)D and HbA1C levels. There was a direct and significant correlation in the second trimester of pregnancy. Based our findings, there was a significant and inverse correlation between serum levels of 25(OH)D in early pregnancy and HbA1C level in the first trimester of pregnancy and there is a direct and significant correlation between serum levels of 25(OH)D in early pregnancy and HbA1C level in the second trimester of pregnancy. It means that in the first trimester of pregnancy, serum levels of 25(OH)D reduced with the increase of HbA1C levels while in the second trimester of pregnancy, the level of serum of 25(OH)D reduced with the decrease of HbA1C levels. There was a significant correlation between serum levels of 25(OH)D and postprandial glucose levels in the second trimester of pregnancy. In fact, at the end of pregnancy, the amount of resistance to insulin reaches to the highest level and in the case, vitamin D have impact on the insulin secretion, probably with the decrease of vitamin D level, the level of insulin secretion will be reduced as well and this cause increase in the blood sugar. It was shown that there was significant and inverse correlation between serum levels of 25(OH)D in the first and second trimester of pregnancy and serum insulin levels at the end of pregnancy. In other words, the reduction of serum levels of 25(OH)D both at the beginning and at the end of pregnancy increase blood insulin levels in the pregnant women at the end of pregnancy. While serum levels of 25(OH)D in early pregnancy did not change serum insulin levels significantly. In this study, there was not a significant association between serum levels of 25(OH)D in the first trimester of pregnancy and incidence of GDM in the second trimester. Although there was a significant association between decrease of serum levels of 25(OH)D in the second trimester of pregnancy and increase in postprandial blood sugar / glucose, the increase is not enough to make the test of diagnosis of GDM positive. In this study, there was no significant relationship between serum levels of 25(OH)D in the first and second trimester of pregnancy and calcium and serum albumin level (Tables 5, 6).

### Table 3. Levels of Vitamin D in pregnant women the first and second trimester in low-risk and high-risk groups

| Group               | Low risk | High risk | p value |
|---------------------|----------|-----------|---------|
|                     | mean±SD  | mean±SD   |         |
| First trimester     | 26.9±46.2| 21.1±43.1 | 0.58    |
| Second trimester    | 25.5±39.5| 3.17±39.6 | 0.99    |

### Table 4. Relationship between vitamin D and metabolic factors in the first trimester of pregnancy *p<0.05

| Type of test       | mean±SD  | p value |
|--------------------|----------|---------|
| Fasting blood sugar (FBS) | 0.201-   | 0.115   |
| OGTT               | 0.252-   | 0.047*  |
| Calcium            | 0.192    | 0.132   |
| Albumin            | 0.098    | 0.447   |
| HbA1C              | 0.005-   | 0.968   |
| Insulin            | 0.246-   | 0.047*  |

### Table 5. Relationship between vitamin D levels and metabolic factors in the second trimester of pregnancy *p<0.05

| Type of test       | mean±SD  | p value |
|--------------------|----------|---------|
| OGTT*(+)          | 7.7 ± 3.41| 0.206   |
| OGTT(−)           | 4.46±56  |         |

### Table 6. Vitamin D levels in the first trimester of pregnancy based on the incidence of pregnancy diabetes in the second trimester * (Blood sugar two hours after 75 g glucose intake≥155)

| OGTT* (+)         | 0.047*   |
|--------------------|----------|
| OGTT (−)          | 0.007    |

### 4. DISCUSSION

Vitamin D deficiency during pregnancy is associated with adverse outcomes. This is essentially an issue of health worldwide (32). The main sources of vitamin D in the body is diet and supplements containing vitamin D and the production of this vitamin in the skin exposed to sunlight. Biologically active form of vitamin D is 1,25-[OH] 2 D, while the 25-[OH] 2 D is a better indication of vitamin D status in the body as the main mechanism for the renal and non-renal production is 1,25-[OH] 2 D and have a higher half-life and higher blood concentrations than 1,25-[OH] 2 D (27). It is expected that normal level of vitamin D in pregnant women be 18-27 ng in the first trimester and 10-22 ng / ml in the second trimester (30). Accordingly, in the present study, of 155 pregnant women in the first trimester, 96.1 % have an optimal serum levels of 25(OH)D and 3.9% below the optimal level (ng / ml <18), respectively. In the second trimester, of 64 pregnant women 90.6% have Optimal levels of serum levels of 25(OH)D and 9.4% lower than optimal levels (ng / ml <10), respectively. As it is described in the result of this study, decrease of levels of serum levels of 25(OH)D in the second trimester has been very significant comparing to the first trimester of pregnancy. This represents a severe reduction of serum levels of 25(OH)D in the second trimester compared to the first trimester of pregnancy in our study population. It seems that significant reduction of serum levels of 25(OH)D is much higher that can be justified by dilution of blood during pregnancy and following that, decrease of vitamin D concentration. In this study, no significant correlation was observed between serum levels of 25(OH)D and GDM among pregnant women at high and low risk. Unlike previous studies, this study...
has been investigated pregnant women in different gestational age (first trimester and second trimester). Considering to this fact that the physiological condition of the pregnant person (such as blood volume in circulation, blood levels of HCG hormone, the expected levels of vitamin D, etc.) is different in each of this time period, result of this study is likely to be more precise than the similar studies in the past in the indication of the relationship between serum levels of 25(OH)D and blood sugar level of pregnant women. The climate, geography and culture of research community were in a way that reduces the amount of cooperation and participation of pregnant women. In this study, the relationship between serum levels of 25(OH)D and GDM was examined with the aim of effectiveness of vitamin D level on the incidence of this disease. Contrary to what some previous literatures were said on the prevalence of vitamin D deficiency in women with GDM than in normal pregnant women (32-34, 28), this study did not confirm such an outcome. In fact, no significant difference is observed a in serum levels of 25(OH)D in the pregnant women at risk of incidence of GDM in both the first and the second trimester of pregnancy comparing to the pregnant women lack of risk factor. In previous studies, it was only examined the relationship between the vitamin D level and the incidence of GDM and type 2 diabetes and it was not clearly examined the relationship between the level of this vitamin and risk factors of incidence of gestational diabetes. It was found that those pregnant women, who in the second trimester of pregnancy have higher blood sugar level after taking 75 g glucose, have lower serum levels of 25(OH)D.

It should also be noted that recent studies provide no evidence of association between serum 25OHD levels in the first trimester of pregnancy and gestational diabetes (35). In addition, in the second trimester of pregnancy, insulin levels were higher in women who had lower vitamin D levels. Rudnicki and Pedersen described previously considering to this fact that the prescription of vitamin D in pregnant women with gestational diabetes affect glucose and insulin levels and decreases blood sugar and blood insulin level expressed the mechanism of increase in sensitivity to insulin by vitamin D (33). Besides, the effect of vitamin D deficiency on the decrease of insulin secretion in mice and humans as well as the mechanisms of decrease function of cells of pancreatic beta and reduction in glucose tolerance had already been investigated (26). In this study, the incidence of GDM was measured through OGTT test by 75 g of glucose and measurement of blood sugar 2 hours after its intake and that was 14.1 %, which was higher than the prevalence reported in the medical texts (3% to 10%). In this study, there was a significant and inverse relationship between serum levels of 25(OH)D in early pregnancy (first trimester) and HbA1C levels at the same age of pregnancy (first trimester), whereas there is a significant and direct relationship between fasting plasma glucose (unlike some of the previous literature (36)). In other words, those who have lower levels of vitamin D at the time of pregnancy had higher levels of HbA1C, but lower level of fasting blood glucose levels in the first trimester of pregnancy, and vice versa. This is perhaps because at the beginning of pregnancy, secretion of hormones such as GH, ACTH, and cortisol influence blood sugar and interfere in the assessment of the relationship between vitamin D and blood sugar levels. Previously, several studies have investigated the relationship between vitamin D and HbA1C (37, 28). For example in 2009, a case-control study has carried out by Alamolhoda and colleagues on 60 pregnant women in the case group and 61 women with no history of disease as the control group (38). However, it was found that there is a inverse relationship between vitamin D levels in the first trimester and HbA1C level in the second trimester of pregnancy. Since HbA1C blood sugar is the best predictive factor of blood sugar, probably the measured HbA1C in the first trimester of pregnancy has been associated with blood sugar level pre-pregnancy and as far as these women has been referred to many gynecologists for their prenatal care, probably vitamins supplementation intake before doing experiments associated with the second trimester of pregnancy. Although in this study no clearly significant association between serum levels of 25(OH)D and risk of GDM was found, according to what was explained in this study, we can probably confirm partly what come in earlier literature in connection with significant relationship between low serum levels of 25(OH)D and increase in blood sugar level and insulin resistance in pregnancy.

5. CONCLUSION

Evidence suggests a possible role of vitamin D deficiency in the pathogenesis of type 2 diabetes. Changes in serum levels of 25(OH)D or function of this vitamin in the body maybe influence insulin allergy (allergic reaction to insulin), pancreatic beta cell function or both of them. In addition, it has been found that several genes are associated with vitamin D in the pathogenesis of this disease. Therefore, vitamin D and its related immune and metabolic pathways may be involved to the pathogenicity of type 2 diabetes through heredity and environment (39). The possible role of vitamin D in the type 2 diabetic is not completely clear. In addition, more information about this topic may identify new targets for treatment and prevention of this disease. Therefore requires further investigation about this case. Given that the percentage of incidence of pregnant women to vitamin D deficiency in this study was 14.1 % and it is higher than stated in previous studies, it seems that this issue requires special attention to the health of pregnant women in ChaharMahal and Bakhtiari province considering to the prevention of this disease. Regarding to what is said about the relationship between vitamin D, blood sugar and blood insulin levels in the second trimester of pregnancy and also due to the influence of the human placental lactogen (hpl) in competition with insulin in the second trimester, it seems that intake of vitamin D supplements can be very useful for pregnant women not to suffer from GDM.

Acknowledgement: Hereby the authors of this study appreciate the cooperation of the patients and Deputy of research and technology of Shahrekord university of Medical sciences and all those who collaborated in the implementation and completion of this research. This study is the result of a general doctoral dissertation with 1163 code.

CONFLICT OF INTEREST: NONE DECLARED

REFERENCES

1. Harlev A, Wiznitzer A. New insights on glucose pathophysiology in gestational diabetes and insulin resistance. Curr Diab Rep. 2010; 10: 242-247.
2. Jovanovic L, Pettitt DJ. Gestational diabetes mellitus. JAMA. 2001; 286: 2516-2518.
3. Dabelea D, Snell-Bergeon JK, Hartsfield CL, Bischoff KJ, Ham-
A Comparison of Serum Levels of 25-hydroxy Vitamin D in Pregnant Women

man RF, McDuffie RS. Increasing prevalence of gestational diabetes mellitus (GDM) over time and by birth cohort. Diabetes Care. 2005; 28: 579-584.

4. Ferrara A. Increasing prevalence of gestational diabetes mellitus. Diabetes Care. 2007; 30: S141-S146.

5. Hossein-Nezhad A, Maghbbooli Z, Vassigh AR, Larjani B. Prevalence of gestational diabetes mellitus and pregnancy outcomes in Iranian women. Taiwan J Obstet Gynecol. 2007; 46: 236-241.

6. Kjos SL, Buchanan TA. Gestational diabetes mellitus. N Engl J Med. 1999; 341: 1749-1756.

7. Recce EA. The fetal and maternal consequences of gestational diabetes mellitus. J Matern Fetal Neonatal Med. 2010; 23: 199-203.

8. Dror DK. Vitamin D status during pregnancy: maternal, fetal, and postnatal outcomes. Curr Opin Obstet Gynecol. 2011; 23: 422-426.

9. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2007; 92: 2017-2029.

10. Ozfirat Z, Chowdhury TA. Vitamin D deficiency and type 2 diabetes. Postgrad Med J. 2010; 86: 18-25; quiz 24.

11. Chu SY, Callaghan WM, Kim SY, et al. Maternal obesity and risk of gestational diabetes mellitus. Diabetes Care. 2007; 30: 2070-2076.

12. Solomon CG, Willett WC, Carey VJ, et al. A prospective study of pregravid determinants of gestational diabetes mellitus. JAMA. 1997; 278: 1078-1083.

13. Parikh SJ, Edelman M, Uwaifo GI, et al. The relationship between obesity and serum 1,25-dihydroxy vitamin D concentrations in healthy adults. J Clin Endocrinol Metab. 2004; 89: 1196-1199.

14. Cheng S, Massaro JM, Fox CS, et al. Adiposity, cardiometabolic risk, and vitamin D status: the Framingham Heart Study. Diabetes. 2010; 59: 242-248.

15. Holick MF. Vitamin D deficiency. N Engl J Med. 2007; 357: 266-281.

16. Norman AW. From vitamin D to hormone D: fundamentals of the vitamin D endocrine system essential for good health. Am J Clin Nutr. 2008; 88: 491S-499S.

17. Gale CR, Robinson SM, Harvey NC, Jawaid MK, Jiang B, Martyn CN, et al. Maternal vitamin D status during pregnancy and child outcomes. Eur J Nutr. 2008; 49: 1196-1199.

18. Ghossein-Nezhad A, Maghbbooli Z, Vassigh AR, Larjani B. Prevalence of gestational diabetes mellitus and pregnancy outcomes in Iranian women. Taiwan J Obstet Gynecol. 2007; 46: 236-241.

19. Barrett H, McElduff A. Vitamin D and gestational diabetes mellitus. Nutr Rev. 2013; 71: 158-167.

20. Maghbbooli Z, Hossein-Nezhad A, Mirzaei K, et al. Association between retinol-binding protein 4 concentrations and gestational diabetes mellitus and risk of developing metabolic syndrome after pregnancy. Reprod Sci. 2009; 17: 196-201.

21. Ditton-Bligh RJ, McElduff PF, McElduff A. Maternal vitamin D deficiency, ethnicity and gestational diabetes. Diabet Med. 2008; 25: 678-684.

22. Zhang C, Qiu C, Hu FB, David RM, van Dam RM, et al. Maternal Plasma 25-Hydroxy vitamin D Concentrations and the Risk for Gestational Diabetes Mellitus. Plosone. 2008; 3(11): 3753.

23. Morales E, Guzmens M, Llop S, Rodriguez-Bernal CL, Tardon A, et al. Circulating 25-hydroxyvitamin D3 in pregnancy and infant neuropsychological development. Pediatrics. 2012; 130(4): e913-e920. doi: 10.1542/peds.2011-3289

24. Alzaim M, Wood RJ. Vitamin D and gestational diabetes mellitus. Nutr Rev. 2013; 71: 158-167.

25. Maghbbooli Z, Hossein-Nezhad A, Mirzaei K, et al. Association between retinol-binding protein 4 concentrations and gestational diabetes mellitus and risk of developing metabolic syndrome after pregnancy. Reprod Sci. 2009; 17: 196-201.

26. Clifton-Bligh RJ, McElduff PF, McElduff A. Maternal vitamin D deficiency, ethnicity and gestational diabetes. Diabet Med. 2008; 25: 678-684.

27. Zhang C, Qiu C, Hu FB, David RM, van Dam RM, et al. Maternal Plasma 25-Hydroxy vitamin D Concentrations and the Risk for Gestational Diabetes Mellitus. Plosone. 2008; 3(11): 3753.

28. Soheilykhah S, Mojibian M, Rashidi M, Rahim-Saghand S, Safari F. Maternal vitamin D status in gestational diabetes mellitus. Nutr Clin Pract. 2010; 25: 524-527.

29. Makgoba M, Nelson SM, Savvidou M, Mes sow CM, Nicolaides K, Sattar N. First-trimester circulating 25-hydroxyvitamin D levels and development of gestational diabetes mellitus. Diabetes Care. 2011; 34: 1091-1093.

30. Cunningham GF, Leveno KJ, Bloom SL, Haut JC, Rouse DJ, Williams Obstetrics. 23rd Edition. New York: McGraw-Hill; 2010: 1124-1126.

31. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. America: American Diabetes Association. 2012: S67-S70.

32. Abdulbari B, Abdulla OAA, Najah MS. Association between Vitamin D Insufficiency and Adverse Pregnancy Outcome: Global Comparison. International Journal of Women's Health. 2013; 5: 523-531.

33. Rudnicki PM, Molsted-Pedersen L. Effect of 1,25-dihydroxycholecalciferol on glucose metabolism in gestational diabetes mellitus. Diabetes. 1997; 40: 40-44.

34. Maghbbooli Z, Hossein-Nezhad A, Karimi F, Shafaei AR, Larjani B. Correlation between vitamin D3 deficiency and insulin resistance in pregnancy. Diabetes Metab Res Rev. 2008; 24(1): 27-32.

35. Burris HH., Rífas-Shiman ShL, Kleinman K, Litonjua AA, Huh SY, Rich-Edwards JW, et al. Vitamin D Deficiency in Pregnancy and Gestational Diabetes Am J Obstet Gynecol. 2012; 207(3): 182.e1-182.e8.

36. Vasileiou V, Athanasiadou A, Giakoumi A, Papageorghiou G, Zapant E, Alevizaki M, et al. Vitamin D deficiency and isolated fasting hyperglycemia in pregnancy. Endocrine Abstracts. 2010; 22: 315.

37. Karimian N, Heidari T, Alavi M, Afrahkhteh M. Relation between irregular menstruation and gestational diabetes at women referring to healthcare centers in Tehran. Medicine Research. 2006; 30: 329-335.

38. Alamolhoda SH, Karimian N, Hoseinpanah F, AlaviMadj H. Relationship between Maternal Hemoglobin Level in First Trimester with Gestational Diabetes Mellitus. Iranian Journal of Endocrinology & Metabolism. 2011; 11(6): 661-666.

39. Palomer X, Gonzalez-Clemente M, Blanco-Vaca F, Mauricio D. Role of vitamin D in the pathogenesis of type 2 diabetes mellitus. Diabetes, Obesity and Metabolism. 2008; 10: 185-197.