Original Article

Serum Vitamin D levels and gestational diabetes mellitus: analysis of early pregnancy cohort from a teaching hospital of Kashmir Valley

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Abstract

Background and Aims: The association of gestational diabetes mellitus and serum Vitamin D levels in different trimesters of pregnancy has been studied recently. We conducted this study in an prospective observational cohort of well-characterized healthy pregnant women to examine the relationship between 1st trimester Vitamin D levels and Gestational Diabetes Mellitus (GDM) status during pregnancy. **Methods:** All pregnant women attending the out-patient department of Gynecology & Obstetrics, aged less than 35 years, and who were in their first trimester were included in the study. Socio-demographic, anthropometric details, clinical details, food frequency questionnaire and physical activity data was collected using validated pretested questionnaire. **Results:** The comparison between those with GDM and those with normal glucose levels has been illustrated. Women in the GDM are older than those in the non-GDM group. The women in GDM group were taller, heavier and their BMI was greater than those in the non-GDM group. There were no significant differences in dietary intake at baseline between mothers with GDM and those with normal glucose levels. Further, it was found that Vitamin D concentration of <30 nmol/L was found among higher among those with GDM and the relationship was statistically significant. **Conclusion:** There is an association between maternal Vitamin D deficiency and increased risk for GDM in early pregnancy among Kashmiri women.

Keywords: Deficiency of Vitamin D, early pregnancy, GDM, Vitamin D

Introduction

Gestational Diabetes Mellitus (GDM) is one of those markers of glucose impairment which is associated with both defective insulin secretion and insulin resistance.[1] Even the normal pregnancy is characterized by a marked reduction in maternal insulin sensitivity in the second and third trimesters. However, the reduced β cells reserve or their maladaptation to higher insulin demands may lead to the development of GDM. GDM is also one of the leading causes of increased maternal risk and fetal complications during pregnancy.[1] Maternal risks include, an increased cesarean section rates[2], preterm labor[3] while fetal complications comprise of but not limited to macrosomia, respiratory distress syndrome, birth injuries, jaundice and hypoglycemia.[4]

It has been documented that children of mothers with GDM are at a higher risk of developing diabetes and obesity in later part of life as compared to those with non-GDM mothers.[5] Furthermore, it has been seen mothers with GDM have 25% chances of developing full blown diabetes after the period of pregnancy is over.[6]

The association of gestational diabetes mellitus and serum Vitamin D levels in different trimesters of pregnancy has

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been studied in many observational, prospective or nested case-control designs.[7,8] Meta-analysis of many observational studies supported the findings consistent with increased risk of development of GDM in pregnant women with deficiency of Vitamin D.[9] Moreover; many studies have refuted this claim of any association of GDM and plasma Vitamin D deficiency[10] and that of complication arising due to GDM.[11]

Studies from developing countries especially India have estimated a very high prevalence of Vitamin D deficiency among pregnant women ranging from 70-100%,[12] and evidence that Vitamin D supplementation in gestational diabetes patients had beneficial effects on fasting plasma glucose and serum insulin levels.[13] It is necessarily important to evaluate the association of GDM with Vitamin D deficiency in these countries. Therefore, this study, was conducted in an prospective observational cohort of well-characterized healthy pregnant women to examine the relationship between 1st trimester Vitamin D levels and GDM status during pregnancy.

Methodology

This study was prospective observational cohort study of pregnant women conducted at Government Medical College, Baramulla, J&K, India. All pregnant women attending the out-patient department of Gynecology & Obstetrics, aged less than 35 years, and who were in their first trimester were included in the study. The study was carried out from June 2019 to December 2019. All the high risk pregnancies including those with instrumental delivery, multiple fetuses, hypertension, cardiac disease, thyroid disease and TORCH infections were excluded from the study. The study was conducted for a period of 6 months. Convenient sampling method was used to select the study participants. Two hundred ninety subjects had their venous blood sample collected at the time of inclusion in the study. Same number of subjects also had their oral glucose tolerance test performed and then completed a glucose tolerance test (GTT) at mid-pregnancy to confirm the GDM status using International Association of Diabetes and Pregnancy Study Groups (IADPSG) classification of GDM.[14]

The Institutional Ethical committee of Government Medical College, Baramulla approved all study procedures. Written informed consent was obtained from all the study subjects after explaining the objectives and procedures involved in the study. Socio-demographic, anthropometric details, clinical details, food frequency questionnaire and physical activity data was collected using validated pretested questionnaire.

Venous whole blood sample was collected into ethylene diamine tetra acetic acid (EDTA) and plain vacutainers (Becton Dickenson, NJ, USA) by phlebotomist. Blood Hemoglobin concentration was measured using an automated cyanmethaemoglobin technique (ABX Pentra 60 C+, Horiba ABX diagnostics, Darmstadt, Germany). Vitamin D concentrations were measured by Liquid chromatography mass spectrometry (LC-MS/MS, 6460 Triple Quadrupole, Agilent Technologies, CA, USA) in maternal plasma samples at enrollment and in cord blood plasma at delivery. Samples were deproteinized by protein crash method and loaded onto a C18 Guard column (Zorbax Eclipse Plus 2.1 × 12.5 mm, 5 μm, Agilent technologies) to trap the analytes of interest and directed to an analytical column (Poroshell 120 EC-C18, 2.1 × 50 mm, 2.7 μm, Agilent Technologies) maintained at 50°C for further separation. MS was operated in Multiple Reaction Monitoring (MRM) mode for specific transitions of Vitamin D2 [25(OH) D2] and Vitamin D3 [25(OH) D3], along with a deuterated 25(OH) D3 as an internal standard, for relative quantification of Vitamin D2 and D3. Data acquisition and analysis was performed by Mass Hunter Workstation (Version: B.05.01) software (Agilent Technologies, CA, USA). The coefficient of variation of the assay was 1.6%. The OGTT, a screening test for diabetes mellitus was performed during thefirst antenatal visit within the end of the first trimester. After an approximately 8 hours overnight fast, the subject consumed 75 g anhydrous glucose and after 2 hours, a 2-ml venous blood sample was collected in EDTA vacutainer. The blood glucose was estimated by Hexokinase method using Dimensions EXL with LM (Siemens Health Care Diagnostic Ltd) automated analyzer. GTT was performed during mid-pregnancy (between 24-28 weeks of gestation) to confirm the GDM status. Fasting Provisional blood sample was collected, glucose was consumed and blood samples post-dose, 1 and 2 hours apart was collected. GDM was defined using International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria.[14]

Statistical analysis

Continuous data was presented as mean and standard deviation if normally distributed, otherwise as median and interquartile range. Independent-samples t test or $\chi 2$ test was used for categorical variables. Logistic regression was done to find the association between Vitamin D concentration at recruitment and GDM status; adjusted odds ratios (AOR) and 95% confidence interval (95% CI) are reported and two-sided *P* values ($P < 0.05$) were considered statistically significant.

Ethical consideration

The Institutional Ethical committee approved the proposal of the study and all study procedures.

Results

This study was conducted on a subset of pregnant women at Government Medical College, Baramulla. A total of 960 pregnant women attended Department of Gynecology & Obstetrics for ANC Checkup's out of which 290 pregnant women were included in the cohort. The included subjects were initially screened for oral glucose tolerance test (OGTT) at the time of recruitment in the study and followed up with glucose tolerance test (GTT) during the second trimester. Out of the 290 pregnant women recruited, 45 (18.3%) had Gestational Diabetes Mellitus (GDM). The baseline characteristics of the study participants are shown

in Table 1. The comparison between those with GDM and those with normal glucose levels has been illustrated. Women in the GDM are older than those in non-GDM group. The women in GDM group were taller, heavier, and their BMI was greater than those in the non-GDM group. The relationship was statistically significant.

Table 2 also describes the baseline characteristics of the study cohort. There were no significant differences in dietary intake at baseline between mothers with GDM and those with normal glucose levels. There were no differences in the mean hemoglobin concentration and equal numbers of women were anemic in both the groups at recruitment. The physical activity level among the non-GDM group was higher than those with GDM, but the association was not statistically significant.

Vitamin D status at recruitment among the pregnant cohort is shown in Table 3. The study participants were divided into groups based on the cut-offs of Vitamin D levels. The proportion of mothers with GDM was compared between women with Vitamin D severe deficiency (<30 nmol/L) and women without Vitamin D severe deficiency (≥30 nmol/L). It was found that Vitamin D concentration of <30 nmol/L was found higher among those with GDM and the relationship was statistically significant. Association of Vitamin D concentration at recruitment and GDM during pregnancy has been illustrated in Table 4.

When considered as quartiles, the lowest quartile (≤23.6 nmol/L) of Vitamin D concentration at recruitment had a significantly higher proportion of GDM compared to the those in the higher quartiles of Vitamin D (26.08% GDM in the lowest quartile $P = 0.032$. Due to the small sample size, the subjects in the

Table 1: Baseline characteristics of study participants

Parameters	All Data (*n*=290)	Women with GDM (*n*=45)	Women with Normal Glucose Levels (*n*=245)	*p*
Socio-demographic characteristics				
Age (years) ^	24.9±2.7	26.5±3.8	24.2±1.9	0.001*
Education#				
Up to High School	103 (35.5)	12 (11.6)	91 (88.4)	0.47
Up to Secondary School	141 (48.6)	28 (19.8)	113 (80.2)	
University & above	46 (15.8)	5 (10.8)	41 (89.2)	
Parity#				
Nulliparous	156 (53.7)	31 (19.8)	125 (80.2)	0.22
Multiparous	134 (46.2)	14 (10.4)	120 (89.6)	
Socioeconomic Status#				
Upper (I)	22 (7.5)	6 (27.2)	16 (72.8)	0.04*
Upper Middle (II)	128 (44.1)	22 (17.1)	106 (82.9)	
Lower Middle (III)	79 (27.2)	8 (10.1)	71 (89.9)	
Upper Lower (IV)	46 (15.8)	5 (10.8)	41 (89.2)	
Lower (V)	15 (5.1)	4 (26.6)	11 (73.4)	
Anthropometric characteristics				
LMP ^	12.0±1.9	11.4±2.1	11.5±2.3	0.923
Height (cms) ^	158.2±6.3	158.0±5.4	157.3±5.9	0.874
Weight (kgs) ^	59.2±8.7	57.5±7.3	54.2±5.4	0.001*
BMI (kg/m^2) ^	23.2±2.7	23.8±4.2	23.1±2.4	0.002*

^ indicated value as mean±SD, *p-value= <0.05 significant at 95% CI,# indicated n (%)

Table 2: Baseline characteristics of study participants

Parameters	All Data (*n*=)	Women with GDM (*n*=45)	Women with Normal Glucose Levels (*n*=245)	*p*
Dietary intakes				
Energy (kcal/d) ^	1960±470	1885±340	1940±430	0.40
Protein (g/d) ^	58.3±12.4	57.2±10.6	58.1±8.8	0.45
Fat (g/d) ^	52.4±14.2	53.0±16.5	50.3±11.2	0.49
Carbohydrate (g/d)^	301.4±80.4	290.0±67.5	305.5±70.3	0.56
Saturated fat (g/d)^	17.2±7.5	15.1±3.4	17.0±1.2	0.88
Biochemical screening parameters				
Hemoglobin ^	11.5±1.6	11.2±2.1	11.9±1.4	0.55
Anemia (Hb <11 gm%)#	132 (45.5)	29 (21.9)	103 (78.1)	0.26
Anemia (Hb >11 gm%)#	158 (54.5)	16 (10.1)	142 (89.9)	0.10
Screening glucose value (mg/dl)¥	96 (82-117)	105 (85-130)	95 (82-115)	0.24
Physical activity level (PAL)				
PAL ^	1.44±0.12	1.42±0.90	1.46±0.14	0.34

^ indicated value as mean±SD, *p-value= <0.05 significant at 95% CI,# indicated n (%),¥ = CI

2nd, 3rd and 4th quartiles of plasma Vitamin D concentrations were combined to allow for a binary grouping for further analysis (<23.6 nmol/L vs. >23.6 nmol/L).The odds ratio of GDM in the lowest quartile of plasma Vitamin D concentration was 2.01 (95% CI: 1.02, 3.099; $P = 0.032$) compared to the other quartiles (combined). The Adjusted OR for GDM was 2.25 (95% CI: 1.10, 4.38; $P = 0.023$) in the lowest quartile of plasma Vitamin D concentration in a model adjusting for maternal age, education, parity, BMI and physical activity levels at recruitment). The Adjusted OR was 2.31 (95% CI: 1.14, 4.91; $P = 0.022$) when maternal BMI was replaced with weight at recruitment.

Discussion

This study was conducted on a subset of pregnant women at Government Medical College, Baramulla. A total of 290 pregnant women were included in the cohort and were followed until pregnancy outcome. In the present study, a total of 45 (15.5%) pregnant women were diagnosed with Gestational Diabetes Mellitus (GDM). Various studies from India have reported the prevalence of GDM in the range of 3% to 25%.[15,16] The results of our study are as per available studies in the literature. Various studies have found factors like increased maternal age, family history of diabetes mellitus, obesity among pregnant women, history of macrosomia, and glycosuria to be associated with GDM.

Table 3: Percentage of Women with GDM and normal glucose levels across Vitamin D status at recruitment

Parameters	Women with GDM (*n*=45)	Women with normal glucose levels (245)	*p*
Vit D levels (mmol/L)	33.5±16.3^	38.2±18.5^	0.26
Vit D insufficiency (<75 nmol/L)#	45 (100)	236 (96.3)	0.32
Vit D deficiency (<50 nmol/L)#	38 (74.5)	196 (55.5)	0.43
Vit D severe deficiency (<30 nmol/L)#	23 (51.1)	86 (35.1)	0.04*

^ indicated value as mean±SD, *p-value= <0.05 significant at 95% CI, # indicated n (%)

In our study, we found that Vitamin D concentrations in the first trimester of pregnancy were lower among those with GDM.

In our study, 80.6% of the women had plasma Vitamin D concentrations that would classify them to be 'insufficient' and about 51.1% of the women diagnosed to have GDM had Vitamin D concentrations less than 30 nmol/L. Our findings of the association of low maternal plasma Vitamin D concentrations in early pregnancy with an increased risk for GDM is consistent with findings from three separate meta-analyses of published studies,[9,17] emphasizing the pivotal role of Vitamin D in the perinatal period. Studies by Aghajafari *et al.*,[17] and Wei *et al.*,[18] have demonstrated that the risk of GDM increases by 60% in women with Vitamin D deficiency. Another study by Roth *et al.*,[19] has demonstrated that Vitamin D has a beneficial role in reducing the risk of GDM. Another study by Clifton-Bligh *et al.*[20] reported the association of poor glucose control with poor Vitamin D status.

In our study, there was no significant correlation between Vitamin D concentration and GTT values (fasting glucose, at 1 hour and 2 hours). Maghbooli *et al.*,[21] also reported no significant correlation between the Vitamin D concentration and GTT values in their study. which is in alignment with the findings of Maghbooli *et al.*,[21] confirming the association of poor Vitamin D status and the risk of GDM through a negative correlation between serum Vitamin D and fasting plasma glucose, fasting insulin, and insulin resistance. Similarly, the association between serum Vitamin D and glycated hemoglobin (HbA1c), an integrated measure of blood glucose control with GDM was also observed, albeit during the second half of pregnancy.[22] In contrary to this, De-regel *et al.*,[23] reported a null relationship between maternal plasma Vitamin D concentrations and risk of GDM. Factors such as selection bias among the participants, sample collection timings, and methods involved in the estimation of Vitamin D concentration, Vitamin D deficiency classification criteria may be the factors involved for these findings.[24]

Table 4: Association of Vitamin D concentration at recruitment and GDM during pregnancy

Variables	Total	≤23.6 nmol/L	≥23.6 nmol/L	*p*
		Quartile 1 Median IQR/*n*%	Quartile 2-3 Reference category	
Vitamin D, nmol/L¥	33.2 (22.5-43.6)	17.4 (13.2-19.8)	37.2 (31.5-49.6)	<0.001*
	n=290	*n*=69	*n*=176	0.022*
No. GDM/total	45/290	18/69	27/176	
		26.08%	15.34%	
		OR (95%CI)¥		
Unadjusted OR		2.01(1.02-3.99)	1.0	0.032*
Adjusted OR 1		2.25 (1.10-4.38)	1.0	0.023*
Adjusted OR 2		2.15 (1.02-4.45)	1.0	0.034*
Adjusted OR 3		2.19 (1.02-4.28)	1.0	0.033*
Adjusted OR 4		2.23 (1.02-4.78)	1.0	0.012*
Adjusted OR 5		2.31 (1.14-4.91)	1.0	0.022*

*p-value= <0.05 significant at 95% CI,# indicated n (%),¥ =CI. 1 Adjusted odds ratio from a logistic regression model containing seasonality. 2 Adjusted odds ratio from a logistic regression model controlling for seasonality and socio-demographic characteristics (maternal age, education categories, parity categories). 3 Adjusted odds ratio from a logistic regression model controlling for seasonality, socio-demographic characteristics (maternal age, education categories, parity categories) and maternal BMI at recruitment. 4 Adjusted odds ratio from a logistic regression model controlling for seasonality, socio-demographic characteristics (maternal age, education categories, parity categories), maternal BMI and physical activity level at recruitment. 5 Adjusted odds ratio from a logistic regression model controlling for seasonality, socio-demographic characteristics (maternal age, education categories, parity categories), maternal body weight and physical activity level at recruitment

After a thorough search of the literature, several proposed mechanisms indicating an association between the risk of GDM and Vitamin D deficiency have been found. A study by Norman *et al.* 1980 described that Vitamin D modulates pancreatic β-cell function and secretion by binding to its circulating active form of Vitamin D with β-cell Vitamin D receptor and regulating the balance between the extracellular and intracellular β-cell calcium pools.[25]Another study reported that Vitamin D can promote insulin sensitivity by stimulating the expression of insulin receptors and enhancing insulin responsiveness for glucose transport.[1] Since Vitamin D is also known to regulate extracellular calcium, low Vitamin D levels may lead to inadequate intracellular cytosolic calcium, which is required for the insulin-mediated intracellular processes and glucose regulation.[25]

Many factors that could confound the relationship between early pregnancy Vitamin D status and GDM. In our study, on replacing maternal body weight with BMI in the adjusted analysis, we found that the association between Vitamin D concentration and GDM persisted indicating that the women with low Vitamin D levels at recruitment had 2.27 times odds of having GDM. Another confounding factor might be seasonal variation as reported by Haggarty *et al.*[26] In this study, adjusting for the season at the time of recruitment did not change the significant association between Vitamin D status and GDM.

The findings of this study will be helpful for primary care physicians in knowing that there is an increase change of developing GDM among those women who have Vitamin D deficiency during the pregnancy. The primary care physicians can plan diet and treatment protocol based on the investigatory report of Vitamin D levels. It is therefore recommended to include Vitamin D estimation in the first antenatal checkup investigation list and especially determine Vitamin D levels in the first and second trimester of pregnancy. This would help to reduce chances of GDM among high risk women, and eventually lead to decreased maternal and infant morbidity and mortality.

Conclusion

An association between maternal Vitamin D deficiency and increased risk for GDM in early pregnancy among Kashmiri pregnant women is an important finding of this study. We recommend knowing the Vitamin D status for every pregnant woman at their first ANC visit, especially among those with a previous history or family history of diabetes mellitus or GDM.

Summary

In this study, women in the GDM group were older, taller, heavier and their BMI was greater than those in the non-GDM group. There were no significant differences in dietary intake and hemoglobin levels at baseline between mothers with GDM and those with normal glucose levels. The physical activity level among the non-GDM group was higher than those with GDM but Vitamin D concentration of <30 nmol/L was found higher among those with GDM respectively.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Chiu KC, Chu A, Go VLW, Saad MF. Hypovitaminosis D is associated with insulin resistance and β cell dysfunction. Am J Clin Nutr 2004;79:820-5.
2. Gorgal R, Gonçalves E, Barros M, Namora G, Magalhães Â, Rodrigues T, *et al.* Gestational diabetes mellitus: A risk factor for non-elective cesarean section. J Obstet Gynaecol Res 2012;38:154-9.
3. Barrett H, McElduff A. Vitamin D and pregnancy: An old problem revisited. Best Pract Res Clin Endocrinol Metab 2010;24:527-39.
4. Carrapato MRG. The offspring of gestational diabetes. J Perinat Med 2003;31:5-11.
5. Pettitt DJ, Aleck KA, Baird HR, Carraher MJ, Bennett PH, Knowler WC. Congenital susceptibility to NIDDM. Role of intrauterine environment. Diabetes 1988;37:622-8.
6. Sivaraman SC, Vinnamala S, Jenkins D. Gestational diabetes and future risk of diabetes. J Clin Med Res 2013;5:92-6.
7. Park S, Yoon HK, Ryu HM, Han YJ, Lee SW, Park BK, *et al.* Maternal Vitamin D deficiency in early pregnancy is not associated with gestational diabetes mellitus development or pregnancy outcomes in Korean pregnant women in a prospective study. J Nutr Sci Vitaminol (Tokyo) 2014;60:269-75.
8. Lacroix M, Battista MC, Doyon M, Houde G, Ménard J, Ardilouze JL, *et al.* Lower Vitamin D levels at first trimester are associated with higher risk of developing gestational diabetes mellitus. Acta Diabetol 2014;51:609-16.
9. Zhang MX, Pan GT, Guo JF, Li BY, Qin LQ, Zhang ZL. Vitamin D deficiency increases the risk of gestational diabetes mellitus: A meta-analysis of observational studies. Nutrients 2015;7:8366-75.
10. Makgoba M, Nelson SM, Savvidou M, Messow CM, Nicolaides K, Sattar N. First-trimester circulating 25-hydroxyVitamin D levels and development of gestational diabetes mellitus. Diabetes Care 2011;34:1091-3.
11. Farrant HJW, Krishnaveni G V., Hill JC, Boucher BJ, Fisher DJ, Noonan K, *et al.* Vitamin D insufficiency is common in Indian mothers but is not associated with

gestational diabetes or variation in newborn size. Eur J Clin Nutr 2009;63:646-52.

12. Ritu G, Gupta A. Vitamin D deficiency in India: Prevalence, causalities and interventions. Nutrients 2014;6:729-75.
13. Kazemi A, Sharifi F, Jafari N, Mousavinasab N. High prevalence of Vitamin D deficiency among pregnant women and their newborns in an iranian population. J Women's Heal 2009;18:835-9.
14. Metzger BE. International Association of Diabetes and Pregnancy Study Groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676-82.
15. Seshiah V, Balaji V, Balaji MS, Paneerselvam A, Kapur A. Pregnancy and diabetes scenario around the world: India. Int J Gynecol Obstet 2009;104(Suppl.):S35-8.
16. Grewal E, Kansara S, Kachhawa G, Ammini AC, Kriplani A, Aggarwal N, *et al.* Prediction of gestational diabetes mellitus at 24 to 28 weeks of gestation by using first-trimester insulin sensitivity indices in Asian Indian subjects. Metabolism 2012;61:715-20.
17. Aghajafari F, Nagulesapillai T, Ronksley PE, Tough SC, O'Beirne M, Rabi DM. Association between maternal serum 25-hydroxyVitamin D level and pregnancy and neonatal outcomes: Systematic review and meta-analysis of observational Studies. BMJ 2013;346:1-14.
18. Wei SQ, Qi HP, Luo ZC, Fraser WD. Maternal Vitamin D status and adverse pregnancy outcomes: A systematic review and meta-analysis. J Matern Neonatal Med 2013;26:889-99.
19. Roth DE, Leung M, Mesfin E, Qamar H, Watterworth J, Papp E. Vitamin D supplementation during pregnancy: State of the evidence from a systematic review of randomised trials. BMJ 2017;359:j5237.
20. Clifton-Bligh RJ, McElduff P, McElduff A. Maternal Vitamin D deficiency, ethnicity and gestational diabetes. Diabet Med 2008;25:678-84.
21. Balducci S, Sacchetti M, Haxhi J, Orlando G, D'Errico V, Fallucca S, *et al.* Physical Exercise as therapy for type II diabetes. Diabetes Metab Res Rev 2014;32:13-23.
22. Lau SL, Gunton JE, Athayde NP, Byth K, Cheung NW. Serum 25-hydroxyVitamin D and glycated haemoglobin levels in women with gestational diabetes mellitus. Med J Aust 2011;194:334-7.
23. Bärebring L, Schoenmakers I, Glantz A, Hulthén L, Jagner Å, Ellis J, *et al.* Vitamin D status during pregnancy in a multi-ethnic population-representative Swedish cohort. Nutrients 2016;8:1-11.
24. Mahalakshmi M, Bhavadharini B, Maheswari K, Anjana R, Jebarani S, Ninov L, *et al.* Current practices in the diagnosis and management of gestational diabetes mellitus in India (WINGS-5). Indian J Endocrinol Metab 2016;20:364-8.
25. El Lithy A, Abdella RM, El-Faissal YM, Sayed AM, Abdel Samie RM. The relationship between low maternal serum Vitamin D levels and glycemic control in gestational diabetes assessed by HbA1c levels: An observational cross-sectional study. BMC Pregnancy Childbirth 2014;14:1-6.
26. Haggarty, P., Campbell, D., Knox, S., Horgan, G., Hoad, G., Boulton, E. *et al.* Vitamin D in pregnancy at high latitude in Scotland. Br J Nutr. 2013;109:898-905.