The Association between Vitamin D Deficiency and Gestational Diabetes

Chesis

Submitted for Partial Fulfillment of Master Degree in Obstetrics & Gynaecology

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First and foremost, Thanks to **Allah**, to whom I relate any success in achieving any work in my life.

I would like to express my deep gratitude and sincere appreciation to **Prof. Dr. Mohammed Ahmed Elkady,** Professor of Obstetrics and Gynaecology, Ain Shams University for his sustained support, continued encouragement and for his precious time and effort that made this thesis possible. It was great honor to me to do this thesis under his supervision.

I owe special feeling of gratitude to **Dr. Dina Yahia Mansour**, Assistant Professor of Obstetrics and Gynaecology, Ain Shams University for her great help, close supervision, wise opinions, guidance and her continuous encouragement and for her precious effort. Without his support, this work would not have been completed.

My deep appreciation to **Dr. Moha Hussein Boshnak**, Assistant Professor of Clinical Pathology, Ain
Shams University for her valuable instructions, unlimited
help and great deal of support, her endless patience with
me and for her experienced guidance and helpful
suggestions that make the completion of this work possible.

A special word of thanks goes to my supportive **mother, Husband, Sons and my daughter** without their help this work wouldn't come to light.

Rana Maher Mohammed



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Abb.	Full term
1,25(OH)2D	1,25 hydroxy vitamin D
ADA	American Diabetes Association
ANC	Antenatal care
ASU	Ain Shams University
BMI	Body mass index
BP	Blood pressure
C section	Caesarian section
Ca	Calcium
cAMP	Cyclic adenosine monophosphate
CLIA	Immunoassays like chemiluminescence
	immunoassays
CVD	Cardiovascular disease
CYP enzymes	Cytochromes P450 enzymes
CYP24A1	Cytochrome P450 Family 24 Subfamily A Member 1
DBP	Vitamin D binding protein
DCs	Dendritic cells
DEQAS	Vitamin D External Quality Assessment Scheme
DGGT	Decreased gestational glucose tolerance
DIPSI	Diabetes in Pregnancy Study Group India
DNA	Deoxyribonucleic acid
EFSA	European Food Safety Authority
EVT	Extravillous trophoblast invasion
FGF23	Fibroblast growth factor 23
FPG	Fasting plasma glucose
g	Gram
GCT	Glucose challenge test
GDM	Gestational diabetes mellitus
GIT	Gastrointestinal tract

Abb.	Full term
НАРО	Hyperglycemia and Adverse Pregnancy Outcome study
HbA1C	Haemoglobin A1c
HFDP	Hyperglycemia first detected during pregnancy
HOMA	Homeostasis model assessment index
HPLC	High performance liquid chromatography
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IADPSG	International Association of Diabetes and Pregnancy Study Groups
IDF	International Diabetes Federation
IFG	Impaired fasting glucose
IGF-1	Insulin-like growth factor type 1
IGT	Impaired glucose tolerance
IIH	Idiopathic infantile hypercalcemia
IL-12	Interleukin 12
IL-1B	Interleukin 1 beta
INF-γ	Interferon-γ
IOM	Institute of Medicine
ISI	Insulin sensitivity index
IU	International units
LBW	Low birth weight
LC-MS/MS	Liquid chromatography, followed by tandem mass spectrometry
LGA	Large for gestational age
MAPK	mitogen-activated protein kinase
MARRS	Membrane-associated rapid response steroid-binding protein
МСНС	Maternal and Child Health Clinics
mg/dl	Millie-gram per dies-liter
Ml	Millie-liter

Abb.	Full term
mmol/l	Millie-mol per liter
mRNA	Messenger RNA
NaPi-IIa	Renal sodium-phosphate co-transporter
NDDG	National Diabetes Data Group
NICE	The National Institute for Health and Care Excellence
NIH	National Institute of Health
NIST	National Institute for Standards and Technology
NIST	National Institute of Standardization Technology
nmol/l	Nano-mol per liter
NR3C1	Nonimprinted glucocorticoid receptor
NS	Non significant
OGTT	Oral glucose tolerance test
OPD	Out patient department
PCOD	Poly cystic ovarian diseases
PG	Plasma glucose
PKC	Protein kinase C
PMCA1b	Calcium extrusion pump
PTH	Parathyroid hormone
PTHR1	Parathyroid hormone type 1 receptor
PTH-rp	Parathyroid hormone related protein
RAP	Receptor-associated protein
RBS	Random blood sugar
RCT	Randomised controlled trials
Rh	Rhesus factor
RIA	Radioimmunoassy
RMPs	Reference Measurement Procedures
S	Significant
SD	Skewed data

Abb.	Full term
SD	Standard deviation
sFlt-1	FMS-like tyrosine kinase 1
SGA	Small for gestational age
Sig	Significance
SNPs	Single nucleotide polymorphisms
SPSS 20	Statistical package for Social Science
T2DM	Type 2 diabetes mellitus
Th1 cytokines	T helper 1 cytokines
Th2 cytokines	T helper 2 cytokines
TLR	Toll-like receptor
TNF-α	Tumor necrosis factor-α
TRPV6	Transient receptor potential cation channel
	subfamily V member 6
UV	Ultra violet rays
VDBP	Vitamin D binding protein
VDR	VITAMIN D receptor
VDRE	Vitamin D response element
VDSP	Vitamin D Standardization Program
VEGF	Vascular endothelial growth factor
WHO	World Health Organization
Wks	Weeks
μg/dl	Micro-gram per dies-liter

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Abstract

Background: Vitamin D deficiency has been identified as a major public health issue, Pregnant women with low 25(OHD) levels have an increased risk of gestational diabetes, pre-eclampsia, small for gestational age infants and low birth weight infants but no association with delivery by Caesarean Section.

Aim of the work: To study the association between vitamin D deficiency and gestational diabetes through measuring vitamin D level in pregnant women with gestational diabetes and controls without gestational diabetes.

Patients and methods: The present study was a case-control study of 87 pregnant women (44 gestational diabetes cases) and (43 controls) in Ain Shams Maternity Hospital from August 2018 to August 2019. Maternal 25(OH)D was measured from 32 to 38 gestational weeks.

We investigated also the relation between vitamin D level and Random blood sugar(in the cases group), mode of delivery, fetal weight as a secondary outcomes. We investigated the correlation between parity, maternal age, gestational age, gender of the baby, maternal blood group, maternal Rh and vitamin D level.

Statistics: The collected data was revised, coded, tabulated and introduced to a PC using Statistical package for Social Science (SPSS 20). Data was presented and suitable analysis was done according to the type of data obtained for each parameter. All the pregnant women in both groups (cases and control) were vitamin D deficient (vitamin D less than 20 mg/ml).

Results: We found no statically significant difference between groups according to vitamin D level, but vitamin D is more deficient in the cases group, a very weak correlation between vitamin D level and random blood sugar level in the cases group (vitamin D does not affect the blood sugar level in the gestational diabetic women), vitamin D level is not affected by parity, maternal age, gestational age, gender of the baby, maternal blood group or maternal Rh. Finally, we found that vit D doesn't affect the mode of delivery but gestational diabetes affect the mode of delivery with increase in the C section to 50% in the cases group in comparison to 4.9% in the control group.

Conclusion: we found no association between vitamin D deficiency and risk of gestational diabetes.

Key words: Vitamin D, Deficiency, Gestational Diabetes

Introduction

vitamin D deficiency has been identified as a major public health issue, which is continuously increasing at a constant rate across the globe. Vitamin D is derived through UV-B-induced synthesis in the skin (Elsori and Hammoud, 2018).

Definition of vitamin D deficiency and insufficiency: Vitamin D deficiency has been defined as a 25(OHD) level less than 20 mg/ml (50 nmol/l) while vitamin D insufficiency is defined as a 25(OHD) level between 21 and 29 ng/ml (52–72 nmol/l). It is a fact that vitamin D deficiency varies by age group; therefore, there are certain controversies in regards of the standardized level for identifying deficiencies. For this purpose, symptomatic approach is widely used for assessing the insufficiency of vitamin D (Holick et al., 2011).

During pregnancy, some women develop insulin resistance, which results in either impaired glucose tolerance (IGT) or gestational diabetes mellitus (GDM), Gestational diabetes mellitus is associated with increased risk for adverse perinatal outcomes, including hypoglycemia, polycythemia, fetal growth disturbances and surgical delivery (Gorgal et al., 2012).

The American Diabetes Association (ADA) defines gestational diabetes mellitus (GDM) as carbohydrate

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intolerance of variable severity, with onset or first recognition during pregnancy (American Diabetes Association, 2004).

Women with GDM have a higher risk of developing diabetes later in life and significantly increased morbidity and mortality (Lee et al., 2007).

Children born to women with pregnancies complicated by GDM are at increased risk for future development of glucose intolerance and obesity (**Bush et al., 2011**).

Pregnant women with low 25(OHD) levels have an increased risk of gestational diabetes, pre-eclampsia, small for gestational age infants and low birth weight infants but no association with delivery by caesarean section (Nassar, 2011).

Evidence suggests that vitamin D is important to glucose homeostasis and insulin sensitivity, potential mechanisms contributing to vitamin D regulation of glucose homeostasis and insulin sensitivity include enhanced insulin secretion and synthesis, reduction in inflammatory processes that reduce functional capacity of pancreatic beta cells, stimulation of the insulin receptors, and enhanced uptake of glucose in muscle and adipose cells (Eliades and Pittas, 2009). Such effects may be due to the influence of genomic (gene and protein expression) and rapid nongenomic effects in pancreatic beta cells, therefore, reduced availability of maternal vitamin D in pregnancy represents a plausible mechanism contributing to the

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development of insulin resistance, leading to IGT and GDM (Wolden-Kirk et al., 2011).

The placenta has an important role for the control of vitamin D during pregnancy. Increased placental expression and production of CYP24A1 may be responsible for the low level of vitamin D that is observed in GDM (Cho et al., 2013).

Women with GDM were shown to have a lower level of vitamin D compared with normal control subjects, and the placental activity of CYP24A1 was increased in GDM compared with normal control placental tissues. These observations provide an alternative to the placental-derived vitamin D metabolism paradigm to explain vitamin D deficiency in GDM. The regulation of CYP24A1 may provide an important target for physiologic interventions that are designed to reduce the risk of adverse pregnancy outcomes related to vitamin D deficiency (Cho et al., 2013).

Vitamin D and omega-3 fatty acids co-supplementation for 6 weeks among GDM patients had beneficial effects on fasting plasma glucose (FPG), serum insulin levels (**Mehri et al., 2017**).

Aim of the Work

This research aims to study the association between vitamin D deficiency and gestational diabetes through measuring vitamin D level in pregnant women with gestational diabetes and controls without gestational diabetes.

Question of the study:

In women with gestational diabetes mellitus does vitamin D level similar to that in controls?

Study hypothesis:

In women with gestational diabetes mellitus vitamin D level may be similar to that in controls.