Effect of Maternal Vitamin D status in Congenital Heart Defects in Offspring: A Case Control Study

Thesis

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By

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Mokhtar Ibrahim Mahmoud

List of Contents

List of Abbreviations

ACE	Angiotensin-converting enzyme
ACOG	American College of Obstetricians and Gynecologists
ARBs	Angiotensin II receptor blockers
ASD	Atrial septal defect
BMI	Body mass index
Ca	Calcium
CARRDIP	Cardiovascular Risk Reduction Diet in Pregnancy
CD	Cesarean delivery
CHD	Congenital heart defect
CoA	Coarctation of the aorta
DHA	Docosahexaenoic acid
DILV	Double inlet left ventricle
DORV	Double outlet right ventricle
EPA	Eicosapentaenoic acid
FGR	Fetal growth restriction
GDM	Gestational diabetes mellitus
HLHS	Hypoplastic left heart syndrome
HRHS	Hypoplastic right heart syndrome
IAA	Interrupted aortic arch
IFN-γ	Interferon gamma
IL	Interleukin
IU	International unit
LCPUFAs	Long-chain polyunsaturated fatty acids
Ml	Milliliter

MYH6	α-myosin heavy chain
Ng	Nanogram
P	Phosphorus
PAPVC	Partial anomalous pulmonary venous connection
PBF	Pulmonary Blood Flow
PDA	Patent ductus arteriosus
PTH	Parathormone
RDAs	Recommended daily allowances
SD	Standard deviation
SGA	Small for gestational age
SGA	Small for gestational age
SPSS	Statistical package for social science
SS	Scimitar syndrome
TAPVC	Total anomalous pulmonary venous connection
TGA	Transposition of great arteries
Th1	T helper 1
TNF-α	Tumor necrosis factor-alpha
TVA	Tricuspid Valve abnormalities
UVB	Ultraviolet B
VACTERL	Vertebral defects, anal atresia, cardiac defects, tracheo-esophageal fistula, renal anomalies, and limb abnormalities
VDD	Vitamin D deficiency
VDR	Vitamin D Receptor
VSD	Ventricular septal defect

List of Tables

List of Figures

Abstract

Background: Interactions between genetic and environmental factors, including modifiable maternal nutrition and lifestyle, play a significant role in the pathogenesis of most congenital heart defects (CHD). The aim of this study was to investigate associations between periconceptional maternal vitamin D status and the prevalence of CHD in offspring.

Methods: A case-control study was performed in 36 mothers of a child with CHD and 37 mothers of a child without CHD from Ain Shams University Children Hospital in the period between January 2019 and June 2019. Maternal blood was obtained to determine serum 25-hydroxyvitamin D. The 25-hydroxyvitamin D concentration was stratified into a deficient<20 ng/ml, moderate deficiency 21-29 ng/ml and adequate >30 ng/ml status above 150 ng/ml presents high risk of toxicity.

Results: Our study showed statistically significant difference between groups according to maternal vitamin D level in ng/ml within 29 days postpartum. Mean vitamin D level in Group 1 (Mothers with congenital heart anomalies in offspring) was 18.35 ng/ml however mean maternal vitamin D level of controls Group 2 (mothers with no congenital anomalies in offspring) was 30.57 ng/ml. In the Group 1 63.9% of mothers had deficient vitamin D level, 16.7% had moderate deficiency and only 19.4 % had an adequate level of vitamin D. On the other hand in the Group 2 37.8% of mothers had deficient vitamin D level, 10.8% had moderate vitamin D deficiency and 51.4% of mothers had an adequate vitamin D level and there were no mothers with toxic level of vitamin D which shows the strong statistically significant relation between maternal vitamin D level and Congenital heart anomalies in offspring.

Conclusion: A compromised maternal vitamin D status is associated with an increased prevalence of CHD in offspring. Therefore, improvement of the periconceptional maternal vitamin D status is recommended.

Key words: Vitamin D, Congenital heart anomalies, Echocardiography

INTRODUCTION

Vitamin D is not only a lipid-soluble vitamin, but also a steroid hormone that can be synthesized endogenously. It has an important role in calcium (Ca)-phosphorus (P) homeostasis and its deficiency causes rickets in children and osteomalacia in adults. Vitamin D deficiency may also result in impairment of immune function, predisposition to cancer, cardiovascular disease, diabetes, rheumatic disease, muscle weakness, chronic pain and neuropsychiatric dysfunction ***(Holick, 2006)***.

The lack of vitamin D during pregnancy is the most important risk factor for infantile rickets and may also result in poor fetal growth and neonatal development. In addition, its deficiency in pregnant women may predispose to gestational diabetes mellitus and preeclampsia ***(Kulie et al., 2015)***.

Vitamin D deficiency (VDD) is identified as a public health problem in many countries, and pregnant women have been identified as a high-risk group, among whom the prevalence of VDD ranges between 20 and 40%. While it is acknowledged that vitamin D supplementation is effective in preventing the VDD, many children are born with this deficiency, raising questions as to how and why VDD affects the pregnancy, the fetus and the newborn's health ***(Naeem, 2010)***.

The increase in the number of studies on this subject shows conflicting results on the association between

25(OH)D levels in pregnancy and adverse effects on maternal and fetal health, both skeletal and non-skeletal (autoimmune diseases, cardiovascular diseases, diabetes and certain types of cancer through "fetal imprinting") Thus, it is advisable to review VDD in mothers and their children so that strategies can be implemented to prevent VDD in pregnancy and lactation, in order to prevent its impact on the fetus, the newborn and in childhood, aiming at a possible reduction in the future development of chronic diseases in adulthood ***(Kalra et al., 2012)***.

Congenital heart defects (CHD) are the most common congenital malformations. The birth prevalence rate of CHD is 9.1 per 1000 live births worldwide and accounts for almost one-third of congenital malformation-related infant deaths. Only 15% of CHD can be attributed to a known cause, such as genetic factors (trisomies, 22q11 deletion), maternal diabetes mellitus, medication, poor nutrition and obesity. It is assumed that interactions between genetic and environmental factors including modifiable maternal nutrition and lifestyle play a significant role in the pathogenesis of most CHD ***(Botto et al., 2014)***.

Previously, it has been reported that maternal multivitamin supplement use in early pregnancy is associated with a reduced risk of CHD in the offspring. This is supported by the estimated 70% reduction of CHD risk in mothers with a strong adherence to a one carbon dietary pattern characterized by fish and seafood.

Conversely, deranged maternal lipid profiles, a high dietary intake of saturated fats, vitamin A or vitamin E are associated with CHD in offspring ***(Pérez-López et al., 2015)***.

Although many studies have been performed focusing on the associations between maternal vitamin D status and pregnancy complications, e.g. gestational diabetes. We hypothesized that the maternal vitamin D status is inversely associated with the prevalence of CHD, modified by the maternal lipid status. Here we investigated this association in a population-based case-control study in Ain Shams University Hospitals.

Aim of the Work

Research Question:

Is Prevalence of Congenital Heart Defects in neonates born to mothers with periconceptional Vitamin D deficiency more than the Prevalence of Congenital Heart Defects in neonates born to mothers with normal periconceptional levels of Vitamin D?

AIM:

This study aimed to study the relation between Maternal Vitamin D status and prevalence of Congenital Heart Defects in their Offspring.