The Relation of Vitamin D Deficiency with Neural Tube Defect Pregnancies

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Abstract:

Background: Neural tube defects NTDs constitute a major health burden (0.5-2/1000 pregnancies worldwide), and remain a preventable cause of neonatal and infant death. Vitamin D is fat soluble, primarily involved in the metabolism of calcium, phosphorus and regulates bone minerilization.

***Objective of This Study*: ** To assess the relation between low serum Vitamin D level in pregnancies complicated by NTDs in comparison with normal pregnancies.

***Patients and Methods*: ** A case- control study, carried out in Salaheddin General Hospital from February 2017 to the September 2017. This study involved 30 pregnant women whose pregnancies were complicated by NTDs and 30 women with normal pregnancies with assessment of vitamin D in each group.

***Results*: ** Low serum vitamin D level was found in 26 women (86.7%) had severe vitamin D deficiency and 4(13.3%) had moderate Vitamin D deficiency of the cases and 6 (20%) of the controls had moderate vitamin D deficiency. With a statistical significant at a *p*-value = <0.05. Serum Ca level was found to be a low in (100%) of those with NTDs pregnancies cases group, while it was low in (7%) of control group. There was a significant relationship between the presence of NTDs and low serum Ca at a *p*- value = <0.05.

Conclusions: In this study there is an association between NTDs and low serum vitamin D levels, adding to the evidence about the importance of nutritional and maternal health factors in the etiology of this disease. Vitamin D supplementation can be advised for the further decrease in the recurrence and occurrence of NTDs.

Keywords: NTDs, VIT D deficiency, BMI.

Introduction:

Neural tube defect (NTDs) is common complex multifactorial disorders in the neurulation of the brain and spinal cord that occur during the early embryonic development [1]. The incidence of open NTDs is nearly occurring in 1 in 1000 pregnancies and vary in different parts of the world depending on the gender of the affected infants, ethnicity, socioeconomic status of the parents, maternal age, parity and abortion [2]. Both genetic and environmental factors, such as maternal vitamin status, have been proposed to affect the risk for NTDs [3].

Anencephaly is the most severe defect; it is always lethal and characterized by absence of the brain and cranium above the base of the skull and orbits [4].

Cephalocele also termed encephalocele- is a herniation of meninges and brain tissue through a defect in the cranium, typically an occipital midline defect. Spina bifida is an opening in the vertebrae through which ameningeocele sac may protrude. In ninety percent of cases, the sac contains neural elements, and the anomaly is termed as meningeomylocele. When meningeal sac alone protrudes through the defect, it is a meningeocele [5].

Vitamin D is primarily involved in the metabolism of calcium, phosphorus and regulates bone mineralization. Vitamin D is a fat-soluble vitamin and provides intestinal absorption of calcium by increasing vitamin D- dependent calcium-binding proteins [6]. The main source is sunlight induced synthesis in the skin [7].

Vitamin D deficiency has been defined a 25 (OH) VitD3 of less than 20 ng/ml. Vitamin D insufficiency has been defined as a 25(OH) VitD3 of 21-30 ng/ml [8].

Pregnant and lactating women require at least 600IU/d of Vitamin D and it had been recognized that at least 1500-2000 IU/d of vitamin D may be need to maintain a blood level of 25 (OH)VitD3 above 30ng/ml [8]. There is accumulating evidence that vitamin D plays a role in the central nervous system (CNS) [9].

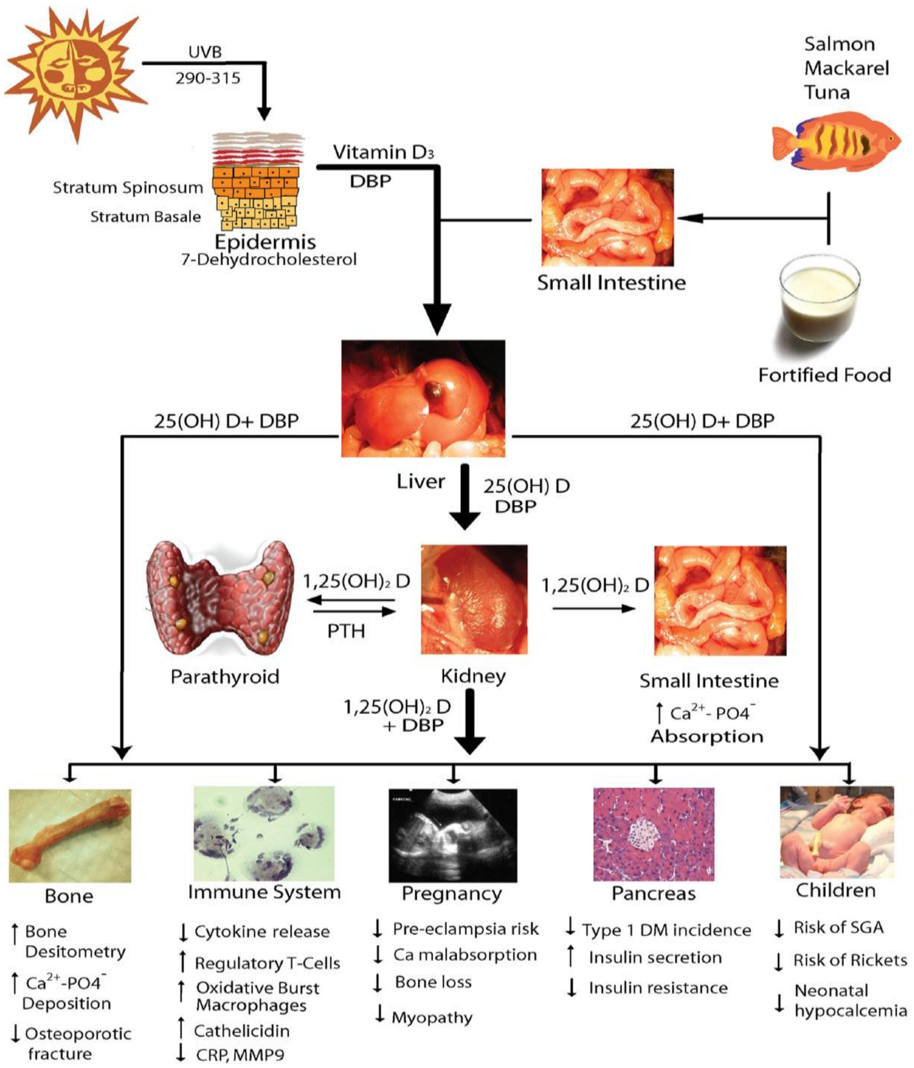

Figure (1-1): Vitamin D metabolism and tissue actions [10] 25 (OH) D = 25-hydroxy vitamin D, Ca^{2+}= calcium; CRP = C reactive protein DBP = Vitamin D binding protein DM = diabetes mellitus, MMP9 = matrix metalloproteinase 9, PO4,= phosphate; PTH = parathyroid hormone SGA = small for gestational age, UVB = ultraviolet B.

Objective of the study:

To measure and identify the relationship between the serum level of 25-OH D3 in both the pregnant women with fetuses complicated by NTDs and the pregnant women with normal pregnancies.

Patients and methods

A case - control study carried out at Obstetrics and Gynecology Unit in Salaheddin General Hospital /Tikrit city - Iraq from the 1st of February 2017 to end of September 2017. A verbal consent was taken from each woman in the case and control group included in this study. The case group comprised of 30 pregnant women whose pregnancies were terminated as a result of second or third trimester ultra-sonographic diagnosis of neural tube defects. The control groups were 30 women who had normal ultra sound findings in the second or third trimester with documented normal fetus.

The venous blood was obtained from each case and control women by venipuncture using disposable syringes at the time of interview in the second or the third trimesters and Vitamin D concentration was determined using (IDS, U.K.) according to the manufacture's instruction.

In this study, we excluded each pregnant woman with any of the following: epilepsy, diabetes mellitus, hypertension, severe anemia or history of previous sibling with NTDs.

The Statistical Package for Social Sciences (SPSS, version 18) was used for data entry and analysis. Chi (χ^2) square test and t-test were used to compare proportions of different factors among different groups of study sample. P value of ≤ 0.05 was regarded as statistically significant.

Results:

The total sample was 60 pregnant women, thirty women with abnormal conceptive product compared with 30 women with normal conceptive product. The minimum age was 16 years and maximum was 43 years, the minimum parity is 0 and maximum was 5, as it is shown in table (1).

The Meningeocele was the most common type of abnormality 8(26.7%), followed by Meningcomylocele 7(23.3%), as shown in table (2).

Severe deficiency was found among 26(86.7%) of cases, moderate deficiency among 4(13.3%) of cases versus 6(20%) of the controls, this relation was statistically significant as shown in table (3).

The S. Ca level was<8.4 mg/dl (low) among 30(100%) of cases versus 7(23.3%) of the controls, this relation was statistically significant as in table (4).

There were significantly strong positive correlation (r) among vitamin D3 level and S. Ca level (0.78) significantly negative correlation among BMI of the mother and Vit.D3 (0.4) and significantly negative correlation among BMI of the mother and S.Ca (0.352), as shown in table (5).

Table (1): The general characteristics of the sample.

Characters	Minimum	Maximum	Mean	Std. Deviation
Age (years)	16	43	30.28	7.00
Gestational(weeks)	18	40	29.45	5.64
Gravity	1	8	3.87	2.07
Abortion	0	3	1.25	1.02
BMI**	18	32	25.13	3.68
Parity	0	5	1.62	1.50

** BMI=body mass index

Table (2): The types of NTDs among study sample.

Abnormality	Case	Control	P value**
Normal	0 (0%)	30 (100%)	<0.05
Meningeocele	8 (26.7%)	0 (0%)	
Meningcomyloce	7 (23.3%)	0 (0%)	
Anencephaly	6 (20%)	0 (0%)	
Anencephalocele	2 (6.7%)	0 (0%)	
Spina bifida occulta	3 (10.0%)	0 (0%)	
Myelocele	2 (6.7%)	0 (0%)	
Occi petal encephalocele	1 (3.3%)	0 (0%)	
Hydrocephalus	1 (3.3%)	0 (0%)	
Total	30 (100%)	30 (100%)	

**statistically significant<0.05, P=P value.NTD = neural tube defect

Table (3): The vitamin D3 level among study sample.

Vit D 3 level	case	control	**P value
<10 ng /ml (Severe deficiency)	26 (86.7%)	0 (0.0%)	< 0.05
10-20 ng/ml (moderate deficiency)	4 (13.3%)	6 (20.0%)	
>20-30 ng/ml (insufficiency)	0 (0.0%)	11 (36.7%)	
>30ng/ml(normal)	0 (0.0%)	13 (43.3%)	
Total	30 (100.0%)	30 (100.0%)	

**statistically significant <0.05, P=P valu

Table (4): The S.calcium level among study sample.

s.ca level	case	control	**P value
(8.4-10.2) mgldl	0 (0.0%)	23 (76.7%)	< 0.05
< 8.4 mg/dl	30 (100.0%)	7 (23.3%)	
Total	30 (100.0%)	30 (100.0%)	

**statistically significant <0.05, P=P value.

Table (5): The correlation of vitamin D3, S.ca level with different characteristics study sample.

		Vit D 3	S.ca
age	R	-0.109-	-0.142
	P	0.407	0.280
Gestational age	R	0.152	0.091
	P	0.247	0.487
gravity	R	-0.038-	-0.035-
	P	0.776	0.790
Parity	R	-0.062-	-0.081-
	P	0.637	0.539
Abortion	R	0.015	0.047
	P	0.909	0.719
BMI	R	-0.4**	-0.352-**
	P	0.002	0.006

**statistically significant <0.05, P=P value, R= value of correlation

Discussion:

NTDs are one of the most common birth defects which are not well understood and have genetic and environmental factors [11, 12].

Increasing parity of the mother and maternal age are important risk factors for NTDs as that found by Whitman *etal* [13]. (2000), who included in their study 644 women diagnosed with NTDs in oxford, England between 1970-1981 and they observed a trend of increasing of NTDs with increasing number of pregnancy p-value-0.005, for women with four or more pregnancy, the risk of NTDs was significantly elevated 1.7 times over that for women with no previous pregnancies. Women aged more than 35 years had a substantially increased risk of having NTDs affected pregnancies, these result are in contrast to our small sample [14].

In this study maternal serum vitamin D level was found to be decreased when gestational age increased and this can be explained by the physiological changes that occur in pregnancy which includes blood volume expansion, hormonal changes, and increased fetal vitamin D requirement for new tissue formation [15]. These results are comparable to that of Ashraf M et al (1999) [16]. Who found that with each trimester there is a progressive decline in serum vitamin D level in normal pregnancy [17]. These finding are in agreement with ZakyTaher*et al* (Turkey/2014), who found that about (81%) of the pregnancies. Had serum vitamin D level ranges between servere to moderate deficiency [12]. In this study it was found (86.71%) of pregnancies complicated by NTD who had severe vitamin D defects and (13%) had moderate vitamin D deficiency. Other researchers, however, reported no relation between vitamin D deficiency and NTDs like Hambidge M *et al*. (1993) [18]. Who stated that "There was no association between serum vitamin D levels and neural tube defects. The explanation for that is the serum vitamin D levels of cases and controls of their study were measured in the first trimester of pregnancy, while in this study measurement them in the second or third trimester, other cause is the study was conducted in a developed country (UK) with higher usual intakes of vitamin D, so the serum vitamin D levels were in the normal range at the time of entry to their study [19]. Concerning the serum calcium level in this study it was found to agree with Buamah PK *et al*. (1984) [20]. Who found that the serum calcium concentrations were lower in the NTDs pregnancies than in the normal control subjects. In this study serum calcium level was low among pregnancies complicated by NTDs. this means strong correlation between vitamin D and calciumdeficiency and NTDs. Obesity is as well known risk factor for 25 (OH) D deficiency [21]. In this study, there was lack of association between 25(OH)D3 level and BMI ,while Yu et al [13] found that there was significant association between vitamin D and BMI [22]. The cause of difference was a small sample. In this study, the BMI was significantly lower among control group, while BMI was high among pregnancies complicated by NTDs [14].

Conclusions: In this study there is an association between NTDs and low serum vitamin D levels, adding to the evidence about the importance of nutritional and maternal health factors in the etiology of this disease. Vitamin D supplementation can be advised for the further decrease in the recurrence and occurrence of NTDs.

Recommendations:

We advice pregnant women with vitamin D levels 30–49 nmol/L, commence 1,000 IU (25μg)/day. Pregnant women with levels < 30 nmol/L should commence 2,000 IU (50μg)/day. Repeat the Vitamin D level at 28 weeks gestation. Pregnant level above 50nmol/L these women should take 400 iu Vitamin D daily as part of a pregnancy multivitamin Consensus-

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