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Original Article

The status of vitamin D in neonates with hypoxic ischemic encephalopathy

Salah M. Saleh[1], Esmat A. Al-Sharkawi[2], Zeinab A. Nasef[1*], Nagwa M. Sabry[1]

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[*]**Correspondence**: Pediatric Department, Faculty of Medicine, Minia University, Egypt

Email: mahmoud2010@live.com

Full list of author information is available at the end of the article.

Abstract

Background: Vitamin D deficiency is a worldwide problem associated with wide spectrum of diseases, ranging from neurological disorders to chronic inflammatory conditions. **Objectives:** This is a cross sectional case control study performed to compare vitamin D serum levels between full term neonates with hypoxic ischemic encephalopathy (HIE) and normal healthy neonates and to determine if there is an association between serum vitamin D levels and neonatal hypoxic ischemic encephalopathy (HIE). **Patients and methods:** This study included 60 full term neonates; 30 of them had the criteria of moderate to severe HIE encephalopathy and the others is clinically free. We measured the serum levels of vitamin D using ELISA in both groups and the mothers of diseased neonates. **Results:** Neonates with hypoxic ischemic encephalopathy had a significant lower (25 (OH) vitamin D) than controls (P-value ≤ 0.001), half of them (50%) had deficient levels of vitamin D, 23.3% had insufficient levels and 26.7 had normal levels of vitamin D. The control group had normal level in 90% and only 10% had insufficient levels of vitamin D and there were significant lower levels in serum maternal vitamin D below normal. **Conclusion:** Full-term neonates with HIE had lower serum levels of vitamin D than healthy neonates with positive correlations between neonatal serum vitamin D levels and their maternal levels.

Key words: BPD, ROP, inotropic support, preterms, mechanical ventilation

Introduction

Hypoxic-ischemic encephalopathy (HIE) is an important cause of acquired neonatal brain injury in term newborn infants and it may lead to neonatal death and long-term disability. Energy failure, membrane depolarization, edema, an increase of neurotransmitter release, the inhibition of neurotransmitter uptake, an increase of intracellular Ca2+, the production of oxygen-free radicals (OFR), lipid peroxidation, and a decrease of blood flow all contribute to the progression of the brain damage that subsequently follows a hypoxic–ischemic insult [1]

Hypoxia-ischemia initially causes energy failure and loss of mitochondrial function. This is accompanied by membrane depolarization, brain edema, an increase of neurotransmitter release and inhibition of uptake, and an increase of intracellular calcium that sets off additional pathologic cascades [2]

Hypoxic ischemic encephalopathy (HIE) is a potentially devastating neonatal brain injury with long-term neurologic effects that affects between 1 and 8/1,000 live birth with the highest rates in developing countries [3].

Vitamin D a key nutrient for children's well-being and growth, is essential for bone health and may contribute to other health benefits [5]

Vitamin D deficiency is a worldwide problem has been associated with wide spectrum of diseases, ranging from neurological disorders to chronic inflammatory conditions [5,6].

The major consequence of vitamin D deficiency

Patients and Methods

This cross sectional case control study was performed to compare vitamin D serum levels between full term neonates with hypoxic ischemic encephalopathy (HIE) and normal healthy neonates and to determine if there is an association between serum vitamin D levels and neonatal hypoxic ischemic encephalopathy (HIE).

The present study was carried out in neonatal intensive care unit (NICU) of Minia University Hospital from April 2017 to December 2017.

This study included 60 full term neonates their gestational ages were 37-40 weeks and postnatal age less than 6 hours. They were classified into 2 groups: First group; included 30 neonates with criteria of moderate to severe hypoxic ischemic encephalopathy as cases and the second group included 30 apparently healthy neonates as controls.

Inclusion criteria of patient group: Full term neonates ≥ 37weeks of gestation of any mode of delivery, both gender who born with perinatal asphyxia or asphyxia required resuscitation as follow: Apger score at 5, 10 minutes afterbirth > 5, fetal acidosis with umbilical artery blood pH > 7 or base deficit

Inclusion criteria for control group: Full term ≥37weeks of gestation neonate who did not require resuscitation, Apgar score on the first and the fifth minutes of life

We excluded from the study: Premature infants (gestational age

All cases and controls were subjected to full carful history, neonatal clinical examination, neonatal laboratory investigations (25(OH) vitamin D by ELISA, complete blood count (CBC) & Reticulocytes count & C-reactive protein (CRP), renal function tests and electrolytes using SYSMEX and arterial blood gases (ABG) by blood gas analyzer. We also measured serum levels of vitamin D in blood of mothers of both groups.

All laboratory investigations were carried out in Clinical pathology department, Minia university hospital.

Ethical considerations

This study was approved from The Ethics Committee of Faculty of Medicine, Minia University, Egypt, and written informed consents were obtained from the parents and they informed about the nature and steps of the study.

Statistical analysis

Data were statistically analyzed using the SPSS software package, version 16 (SPSS Inc., Chicago, IL, USA) on a personal computer. Numerical data were expressed as range, mean± SD, median, and percentiles. Non numerical data were expressed as frequencies. Comparative studies were done using Student t test and chi square test. (p value < 0.05 was considered significant). Pearson correlation test was used to detect correlation between different parameters.

Results

There were no significant differences between cases and controls as regards demographic data (Table 1 & Figure 1). Neonates with hypoxic ischemic encephalopathy had significant lower vitamin D levels than controls (P-value ≤ 0.001), half of them (50%) had deficient levels of vitamin D, 23.3% had insufficient levels and 26.7% had normal levels of vitamin D. The control group had normal level in 90% and only 10% had insufficient levels of vitamin D (Table 2). There were significant lower serum levels of vitamin D in maternal blood of neonates with HIE than controls (Table 2). There were positive correlations between maternal and neonatal serum vitamin levels in neonates with HIE (r = 0.418 and p-value = 0.02*) (Table 3).

Discussion

Our studied neonates with hypoxic ischemic encephalopathy had a significant lower vitamin D than controls (p less than 0.001) as there is 50% (n=15) had a deficient level of vitamin D and 23.3% (N=7) had insufficient level of vitamin D, and 26.7(n=8) had a normal level of vitamin D with p-value less than 0.001 in comparison with control group which had normal level in 90% (n=27) and only 10% (n=3) had insufficient level which is in agreement with two published studies [7,8].

Our results revealed a significant positive correlation between maternal serum vitamin D and its levels in their

neonates with (HIE), this can be explained by the fact that vitamin D stores of the neonate depend entirely on the vitamin D stores of their mothers which is in agreement with other study [9].

There were no significant correlation between neonatal serum levels of vitamin D and gender, mode of delivery, consanguinity or residence in both cases and control groups.

Our results revealed that there is significant difference between case group and control group regarding Apgar score at 1st minute as all case group patients had Apgar score less than 7 as suggested in the inclusion criteria. On the other hand control group had Apgar score more than 8 in first 5 minutes which is in agreement with study of [10].

Also our results revealed significant difference between case group and control group regarding arterial pH after 5 minutes as all case group patients had arterial pH below 7 up to 7,1 as inclusion criteria suggested as there was metabolic acidosis in all HIE case. On the other hand control group had normal arterial pH at 1 and 5 minutes which is in agreement with other reports [10].

Our results revealed that there is significant difference between case group and control group regarding CT finding (Not shown in the results section). There were 76% of our studied cases had a positive findings in CT ranging in severity from brain oedema in 20% of cases to hypoxic changes as hypo density in CT findings in 56.7% of them which is in agreement with others [11,12]. We can recommend - according to the results of this study - more studies for vitamin D supplementation for pregnant women risk of vitamin D deficiency and giving therapeutic dose of vitamin D (1,25 hydroxy) to all pregnant women who are at risk of vitamin D deficiency and also giving vitamin D to all full term neonates with HIE as a therapeutic trial.

Conclusions

Full-term neonates with HIE had lower serum levels of vitamin D than healthy neonates with positive correlations between neonatal serum vitamin D level and their maternal levels.

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Author's contributions

SS and SN conceived the study. NZ revised the patients' medical reports and the final manuscript. SE conducted the laboratory investigations. All authors revised the final draft of the manuscript.

Conflict of interest

The authors have no conflict of interests to declare.

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Author's details

[1]Pediatric Department, Faculty of Medicine, Minia University, Egypt.

[2]Clinical-pathology Faculty of Medicine, Minia University, Egypt.

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Table (1) comparison between cases and control groups regarding demographic characteristics

Item	**Cases N=30**	**Controls N=30**	**P-value**
Gestational age weeks	38.9±1.7	39.1±1.6	0.656
Mothers age in years (mean ±SD)	29.5±7.2	29.1±8.5	0.961
Weight in kg (mean ±SD)	3.2±0.56	3.1±0.53	0.410
Sex: N (%)			0.196
Males	17(56.7%)	12(40%)	
Females	13(43.3%)	18(60%)	
Mode of delivery: N (%)			0.605
NVD	15(50%)	13(43.3%)	
CS	15(50%)	17(56.7%)	
Consanguinity			
Negative	15(50%)	12(40%)	0.43
Positive	15(50%)	18(60%)	

Table (2): Comparison between cases and controls regarding serum vitamin D level and other laboratory tests

Item	Cases N=30	Controls N=30	P-value
pH (mean ±SD)	6.82±0.14	7.39±0.03	<0.001**
BE (mean ±SD)	-15.1±2.3	0.53±2.2	<0.001**
Haemoglobin (gm\dl)	16.1±2.5	16.1±1.8	0.977
TLC (10^3)	(16.2±9.05)	(15.7±5.3)	0.768
Platelets count ($10^{3)}$	(272±144.6)	(327.2±133.3)	0.080
CRP			0.076
Normal	27(90%)	30(100%)	
Abnormal	3(10%)	0(0%)	
Electrolytes:			
Sodium (meq\L)	139±4	140+_4.5	0,97
Potassium (meq\L**)**	4 ±0,5	4,2_+0,7	0,89
Calcium (mg\dl)	8.85±0.3	9±0.5	0.8
Urea (mg\dl)	25.9±10.08	30.03±8.9	0.104
Creatinine (mg\dl)	0.76±0.15	0.58±0,18	<0.001**
Vitamin D(mean ±SD)ng\l	15.2±7.5	25.5±3.2	<0.001**
Mother Vitamin D (ng\l)	18.7 ±7.2	28.01	<0.001**

P value< 0.05: significant.
P value< 0.01: highly significant.

Table (3): Comparison between cases and controls regarding CT finding

Item	Cases N=30	Controls N=30	p-value
Normal	7(23.3%)	30(100%)	<0.001**
Brain edema	6(20%)	0(0%)	
Hypoxia	17(56.7%)	0(0%)	

P value< 0.05: significant.
P value< 0.01: highly significant.

Table (4): Serum vitamin D level in cases and control groups

Item	Cases N=30	Controls N=30	p-value
Normal (≥20ng/ml)	8(26.7%)	27(90%)	<0.001**
Insufficiency (15-20 ng/ml)	7(23.3%)	3(10%)	
Deficiency (<15ng/ml)	15(50%)	0(0%)	

P value< 0.05: significant.
P value< 0.01: highly significant.

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Table (5): Comparison between serum vitamin D level in cases group and their mothers

Item	Cases N=30	Mothers N=30	p-value
Normal (≥20ng/ml)	8(26.7%)	8(26.7%)	0.7
Insufficiency(15-20 ng/ml)	7(23.3%)	10(33.3%)	0.5
Deficiency (<15ng/ml)	15(50%)	12(40%)	0.6

Analysis of qualitative data by Z test, p-value is considered significant at <0.05

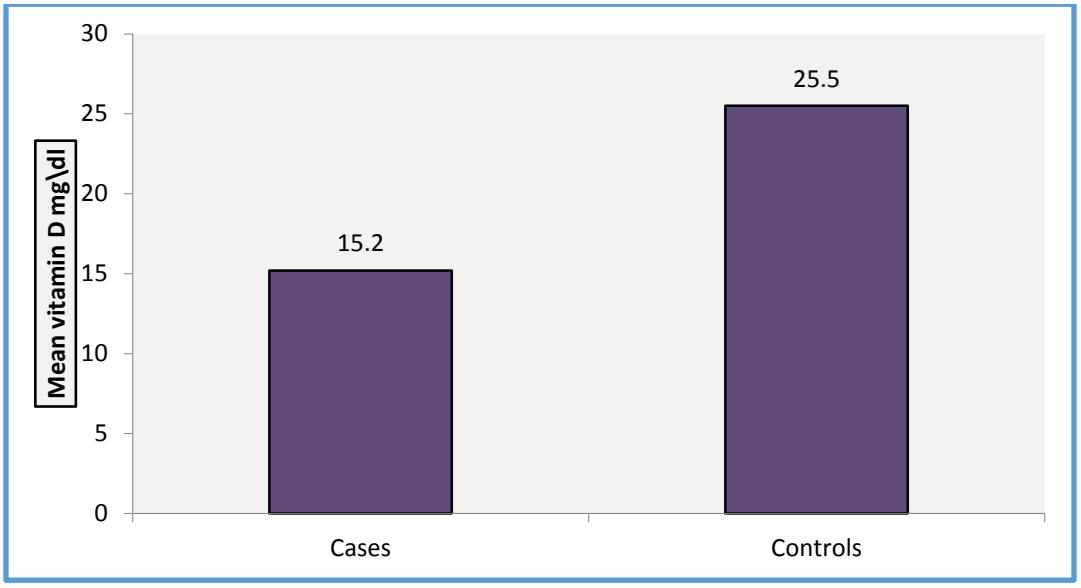

Figure (1) Comparison between cases and controls regarding serum vitamin D level

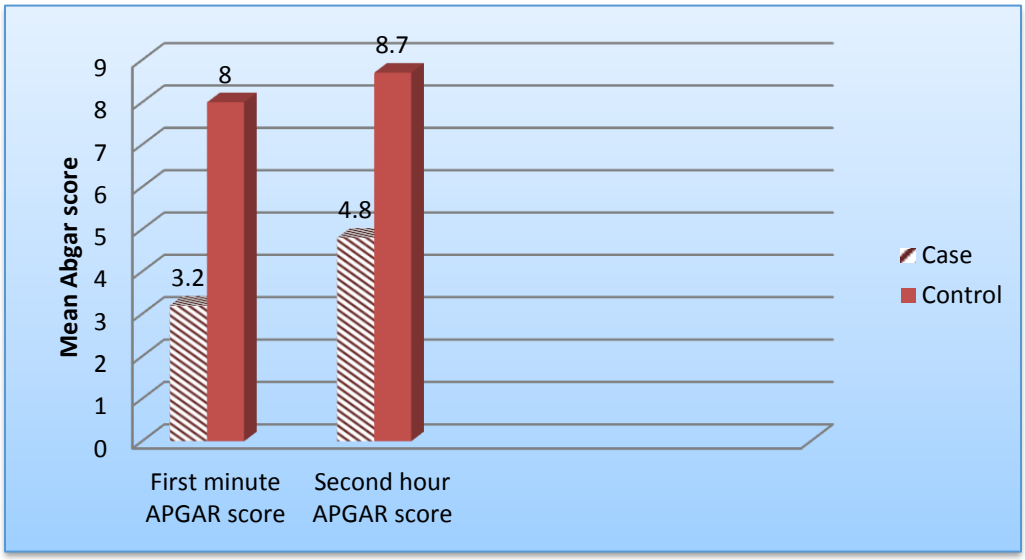

Figure (2) comparison between cases and controls regarding APGAR score

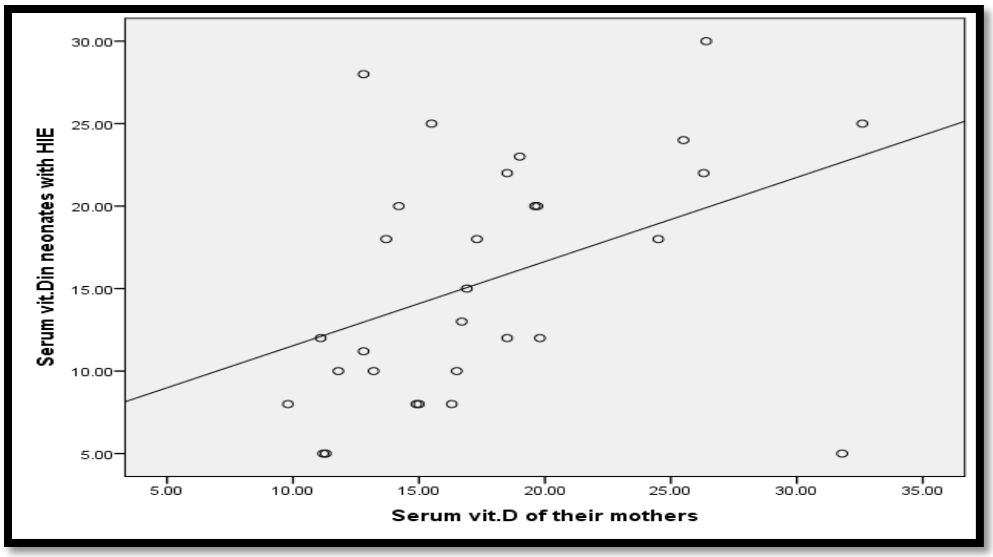

Figure (3) Correlation between serum vitamin D in neonates with hypoxic ischemic encephalopathy and their mothers

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