

# Impact of Oral Vitamin D Supplementation on First Tooth Eruption of Jordanian Premature Infants

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## ABSTRACT

**Objective:** To elucidate the impact of oral vitamin D supplementation on the time (early versus late chronological age) of first tooth eruption in premature infants.

**Method:** A total number of 110 Jordanian preterm infants (gestational age < 37 weeks, and birth weight < 2500 g) who were born and attended the neonatal follow up clinics at Prince Hashim Ben Al-Hussein and Queen Alia Military Hospital / Jordan from April 2012 till March 2014, were included and randomized into three main groups:-

**A-**preterm infants who were fed exclusively breast milk without extra Vitamin D supplementation, **B-**preterm infants who were fed exclusively special preterm formula containing 400 IU vitamin D/100mg, but not supplemented with extra oral vitamin D.

**C-**preterm infants who were fed exclusively special preterm formula containing 400 IU vitamin D/100mg and additionally supplemented with 400 IU of oral vitamin D.

A first tooth eruption record was completed by the principal neonatologist and the parents of the enrolled infants during the annual clinic visits.

**Results:** A total of 110 premature infants (50 males, 60 females,) were included in this study. 44 preterm infants were of gestational age < 32 weeks at birth, and 66 were > 32 weeks gestation at birth. 61 premature babies had a birth weight < 1.5 kg, and 49 had a birth weight > 1.5 kg. Early tooth eruption occurred in 83 of the total 110 studied preterm infants (32, 24, and 27 infants from groups A, B, and C respectively), and 27 (8, 11, and 8 infants from groups A, B, and C respectively) have had late first tooth eruption. The mean number of breast fed infants with early tooth eruption ( who had the least content of vitamin D in milk ) is significantly more than the means of the other two groups ( $P$  - value = 0.036 ). The mean number of infants in the three groups with late tooth eruption is not significantly different ( $P$ - value = 0.269). Comparing the breast fed infants with different gestational ages, and different birth weights with the infants in the other two groups in respect to early versus late first tooth eruption, no statistically significant effect of increased vitamin D content more than the breast milk content could be found.

**Conclusion:** There is clear evidence that extra supplementation with oral vitamin D has no effect on the time of first tooth eruption of premature infants.

**Key words:** Tooth eruption, Premature, Vitamin D.

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## Introduction

Vitamin D is a fat-soluble vitamin that plays an important role in bone metabolism. It is also considered a steroid hormone with pleiotrophic effects, and has important roles in the optimal functioning of many organ systems, and may be a risk modifying factor for many chronic diseases.<sup>(1)</sup>

The vitamin D stores of the newborn depend entirely on the vitamin D stores of the mother, and get approximately 50-70% of the level of the mother.<sup>(2)</sup> Hence, if the mother is vitamin D-deficient, the infant will be deficient because of decreased maternal fetal transfer of vitamin D.<sup>(3)</sup> It has been estimated that breast milk from a vitamin D replete mother contains between 20 and 60 IU/l of vitamin D<sup>(4)</sup> and hence adequate intake of vitamin D cannot be met with human milk as the sole source of vitamin D in a breast-feeding infant.<sup>(4,5)</sup> Most breastfed infants are able to synthesize additional vitamin D through routine sunlight exposure. The nutrition of preterm infants using mineral supplementation has become important, due to the fact that minerals have different functions in the body, although little is known about them. Several studies have demonstrated that preterm infants born <32 weeks (and especially those <28 weeks) are at greater risk of developing vitamin D deficiency compared to more mature infants.<sup>(6,7)</sup>

It was estimated that 55% of extremely low birth weight (ELBW) infants and 23% of Very Low Birth Weight (VLBW) infants have low bone mineralization due to premature birth.<sup>(2)</sup> Influence of preterm birth on teeth development and eruption has been investigated.

Factors related to delayed tooth eruption are thought to include the general delay in the growth development of preterm babies Drummond *et al.* 1992,<sup>(8)</sup> short gestation Golden *et al.* 1981, Seow *et al.* 1988, Fadavi *et al.* 1992,<sup>(9,10,11)</sup> low birth weight Trupkin 1974,<sup>(12)</sup> and neonatal factors, including complications of prematurity, systemic disorders, duration of oral intubation, average weight gain / day etc. Viscardi *et al.* 1994.<sup>(13)</sup> Nutritional factors, postnatal weight gain and growth of the child may also effect the eruption of the deciduous teeth Seow *et al.*, 1988.<sup>(10,14)</sup>

The effect of vitamin D on dentition of premature infants was not studied.

Our study is a prospective longitudinal study of first tooth eruption in Jordanian preterm infant's, presents finding on the relationship between the timing of first tooth eruption in prematurely born infants (early versus late chronological age) and oral vitamin D supplementation.

## Methods

A total number of 110 Jordanian preterm infants (gestational age < 37 weeks and birth weight < 2500 g) who were born in Prince Hashim Ben Al-Hussein Military Hospital. Zarqa/ north of Jordan and Queen Alia Military Hospital were included and followed up until the age of 18 months in the neonatal clinics. According to the study protocol they were stratified according to birth weight and gestational age then randomly assigned to one of three groups to receive vitamin D supplementation either 200, 400 or 800 IU/day. Doses were started from the time of tolerance of full enteral nutrition until 6 months of chronological age, after which they were allowed solid food.

Group A-preterm infants who were fed exclusively breast milk during the first 6 months of age without Vitamin D supplementation, Group B-preterm infants who were fed exclusively special preterm formula containing 400 IU vitamin D/100mg, but not supplemented with extra oral vitamin D. Group C-preterm infants who were fed during the first 6 months of life, exclusively special preterm formula containing 400 IU vitamin D/100mg and additionally supplemented with 400 IU of oral vitamin D.

Vitamin D was supplemented either by using special care premature formula (Similac neosure /Abbot Laboratories), which contained 359 IU/ 100 mg or oral vitamin D drops 400 IU/ drop. All included preterm infants were allowed solid food by the end of the sixth month of life.

A first tooth eruption record, which was approved by the Jordanian Royal Medical Services ethical committee, included the influencing factors of (sex, gestational age, birth weight, weight at the time of the first tooth

eruption, neonatal sepsis, history of oral intubation, feeding history, amount of supplemented vitamin D, history of rickets, presence of chronic medical illnesses, recurrent diarrheal episodes and history of recurrent admissions to the hospital). Data was collected by the neonatologist from medical records, and the parents observations during the follow up scheduled clinic visits. A full explanation of the benefits, risks, procedures and possible discomforts that the infant might face was given to the infants' parents, and their consent was obtained prior to inclusion in the study. The inclusion criteria were: a gestational age of less than 37 weeks, birth weight less than 2.500 kg, normal growth parameters and normal calcium, phosphorous and alkaline phosphatase levels during the study period. Infants with congenital orofacial abnormalities (e.g. cleft palate or cleft lip), chronic medical illnesses (such as chronic lung disease, failure to thrive, congenital hypothyroidism, bone defects and malabsorption states), infants with documented rickets, and preterm infants who had positive blood cultures or intubated for more than 5 days during their admission in the neonatal intensive care unit were excluded. The withdrawal criterions were failure of vitamin D administration according to the protocol or the parents wish to withdraw their baby from the study; but no withdrawals occurred.

Tooth eruption was defined as any part of the crown that penetrated the mucous membrane. It was confirmed by the same dentist who was not informed of the medical history of the infant during the oral examination that was carried out using an artificial light, in the dental clinic at prince Hashem Ben Al-Husseini Military Hospital.

The baby's chronological age was defined as the number of days, weeks, months or years today from his or her actual date of delivery, or birthday. Delayed tooth eruption was considered if the first tooth erupted after the chronological age of 40 weeks, because the first tooth in normal infants erupts between 24 and 40 weeks of age. The premature infant was the unit of analysis in this study. A descriptive

statistical study (mean, standard deviation and cross tabulation) using SPSS version 10 was carried out on the measurements of variables collected. Some data collected in this prospective study were parametric and other data were nonparametric. The Chi-square distribution or one -way ANOVA test Odds ratio, and two- sided 95% confidence intervals where appropriate were used when concerning proportions.

The level of significance was set at  $P < 0.05$ .

Ethical issues were considered and the study was approved of by ethical committee of the Jordanian Royal Medical Services, and an informed consent was obtained from the parents.

## Results

As Table V shows: A total of 110 (50 males, 60 females,) infants were included in this study. 44 preterm infants were of gestational age < 32 weeks at birth, 66 > 32 weeks gestation at birth, 61 with birth weight < 1.5 kg, and 49 with birth weight > 1.5 kg at birth.

Of the 110 preterm infants : 40 ( 16 males, 24 females, 13 preterm infants of gestational age less than 32 weeks at birth, 27 of more than 32 weeks gestation at birth, 16 with birth weight less than 1.5 kg, and 24 with more than 1.5 kg at birth.), 35 ( 17 males, 18 females, 14 preterm infants of gestational age less than 32 weeks at birth, 21 of more than 32 weeks gestation at birth, 22 with birth weight less than 1.5 kg, and 13 with more than 1.5 kg at birth.), and 35 ( 17 males, 18 females, 17 preterm infants of gestational age less than 32 weeks at birth, 18 of more than 32 weeks gestation at birth, 23 with birth weight less than 1.5 kg, and 12 with more than 1.5 kg at birth.) were studied in groups A, B, and C respectively.

In this study of the total 110 studied preterm infants 83 (32, 24, and 27 infants from groups A, B, and C respectively) have had early first tooth eruption (Table I), and 27 (8, 11, and 8 infants from groups A, B, and C respectively) have had late first tooth eruption (Table II).

Using the one -way ANOVA test to compare the effect of different doses of vitamin D

**Table I:** Patients characteristics.

	<b>Breast milk = 200 IU vitamin D. Group - A</b>	<b>Premature formula = 400 IU vitamin D. Group -B</b>	<b>Premature formula+ Vitamin D (total 800 IU vitamin D). Group -C</b>
Total number of patients. n=110	n=40	n=35	n=35
Male. n=50	n=16	n=17	n=17
Female. n=60	n=24	n=18	n=18
Gestational age at birth/weeks:-			
< 32 n= 44	n=13	n=14	n=17
>32 n= 66	n=27	n=21	n=18
Birth weight/Kg;-			
<1.5 n= 61	n=16	n=22	n=23
>1.5 n= 49	n=24	n=13	n=12

**Table II:** Characteristics of preterm infants with early first tooth eruption.

	<b>Breast milk = 200 IU vitamin D. Group -A n=40</b>	<b>Premature formula= 400 IU vitamin D Group- B n=35</b>	<b>Premature formula+ Vitamin D (total 800 IU vitamin D). Group-C n=35</b>
Total number of patients. n=	n=32	n=24	n=27
Male. n=43	n=15	n=15	n=13
< 32 Wk.n=14	n=5	n=4	n=5
> 32 Wk.n=29	n=10	n=11	n=8
<1.5 Kg.n=22	n=5	n=8	n=9
>1.5 Kg.n=21	n=10	n=7	n=4
Female n=40	n=17	n=9	n=14
< 32 Wk.n=11	n=4	n=2	n=5
> 32 Wk.n=29	n=13	n=7	n=9
<1.5 Kg.n=19	n=7	n=5	n=7
>1.5 Kg.n=21	n=10	n=4	n=7
< 32 Wk n=25	n=9	n=6	n=10
Male. n=14	n=5	n=4	n=5
Female. n=11	n=4	n=2	n=5
<1.5 Kg. n=25	n=9	n=6	n=10
>1.5 Kg. n=0	n=0	n=0	n=0
> 32 Wk. n=58	n=23	n=18	n=17
Male.n= 29	n=10	n=11	n=8
Female.n=29	n=13	n=7	n=9
Early Eruption. n=83			
<1.5 Kg.n=16	n=3	n=7	n=6
>1.5 Kg.n=42	n=20	n=11	n=11
<1.5 Kg. n=41	n=12	n=13	n=16
Male.n=22	n=5	n=8	n=9
Female.n=19	n=7	n=5	n=7
< 32 Wk.n=25	n=9	n=6	n=10
> 32 Wk.n=16	n=3	n=7	n=6
>1.5 Kg. n=42	n=20	n=11	n=11
Male.n=21	n=10	n=7	n=4
Female.n=21	n=10	n=4	n=7
< 32 Wk.n=0	n=0	n=0	n=0
> 32 Wk.n=42	n=20	n=11	n=11

**Table III:** Characteristics of preterm infants with late first tooth eruption.

		Breast milk = 200 IU vitamin D Group -A n=40	Premature formula= 400 IU vitamin D Group -B n=35	Premature formula+ Vitamin D (total 800 IU vitamin D). Group -C n=35
Late Eruption. n=27	Total number of patients. n=27	n=8	n=11	n=8
	Male. n=7	n=1	n=2	n=4
	< 32 Wk. n=5	n=0	n=1	n=4
	> 32 Wk. n=2	n=1	n=1	n=0
	<1.5 Kg. n=5	n=0	n=1	n=4
	>1.5 Kg. n=2	n=1	n=1	n=0
	Female. n=20	n=7	n=9	n=4
	< 32 Wk. n=14	n=4	n=7	n=3
	> 32 Wk. n=6	n=3	n=2	n=1
	<1.5 Kg. n=15	n=4	n=8	n=3
	>1.5 Kg. n=5	n=3	n=1	n=1
	< 32 Wk. n=19	n=4	n=8	n=7
	Male n=5	n=0	n=1	n=4
	Female n=14	n=4	n=7	n=3
	<1.5 Kg. n=19	n=4	n=8	n=7
	>1.5 Kg. n=0	n=0	n=0	n=0
	> 32 Wk. n=8	n=4	n=3	n=1
	Male n=2	n=1	n=1	n=0
	Female n=6	n=3	n=2	n=1
	<1.5 Kg. n=1	n=0	n=1	n=0
	>1.5 Kg. n=7	n=4	n=2	n=1
	<1.5 Kg. n=20	n=4	n=9	n=7
	Male n=5	n=0	n=1	n=4
	Female n=15	n=4	n=8	n=3
	< 32 Wk. n=19	n=4	n=8	n=7
	> 32 Wk n=1	n=0	n=1	n=0
	>1.5 Kg. n=7	n=4	n=2	n=1
Male n=2	n=1	n=1	n=0	
Female n=5	n=3	n=1	n=1	
< 32 Wk. n=0	n=0	n=0	n=0	
> 32 Wk n=7	n=4	n=2	n=1	

**Table IV:** Comparison between infants with early first tooth eruption in the three groups.

Male & females	Breast fed Early eruption	Premature formula fed Early eruption	Premature formula fed +Vit.D 400 IU Early eruption
GA < 32W	9	6	10
GA>32W	23	18	17
Mean	16	12	13.5
SD	7	6	3.5
P- value =	0.036		

**Table V:** Comparison between infants with late first tooth eruption in the three groups.

Male & females	Breast fed late eruption	Premature formula fed Late eruption	Premature formula fed +Vit.D 400 IU late eruption
GA < 32W	4	8	7
GA>32W	4	3	1
Mean	4	5.5	4
SD	0	2.5	3
P- value=	0.265		

**Table VI:** Cross tabulation between breast fed and premature formula fed premature infants.

GA <32 weeks	Breast fed 200	Premature formula fed 400	p-value	Odds ratio	95% CI
Early tooth eruption	9 = 69%	6 =43%			
Late tooth eruption	4=31%	8 =57%	0.1739	3.0000	0.6157 to 14.6170
Total	13	14			
GA> 32 weeks					
Early tooth eruption	23 = 85%	18 =86%			
Late tooth eruption	4 =15%	3 = 14%	0.9589	0.9583	0.1898 to 4.8380
Total	27	21			
BW <1.5 kg					
Early tooth eruption	12 = 75%	13 = 59 %			
Late tooth eruption	4 = 25%	9 = 41%	0.3114	0.4815	0.1169 to 1.9825
Total	16	22			
BW >1.5 kg					
Early tooth eruption	20 =83%	11 =85%			
Late tooth eruption	4 =17%	2 =15%	0.9196	0.9091	0.1429 to 5.7817
Total	24	13			
all infants					
Early tooth eruption	32 = 80%	24 = 69%			
Late tooth eruption	8 =20%	11 = 31%	0.2594	1.8333	0.6394 to 5.2566
Total	40	35			

**Table VII:** Cross tabulation between breast fed and premature formula fed + Vitamin D supplemented premature infants.

GA <32 weeks	Breast fed 200	Premature formula fed +Vit.D( 800 IU)	p-value	Odds ratio	95% CI
Early tooth eruption	9 = 69%	10=59%			
Late tooth eruption	4=31%	7=41%	0.5589	1.5750	0.3434 to 7.2245
Total	13	17			
GA> 32 weeks					
Early tooth eruption	23 = 85%	17=94%			
Late tooth eruption	4 =15%	1=6%	0.3512	0.3382	0.0346 to 3.3044
Total	27	18			
BW <1.5 kg					
Early tooth eruption	12 = 75%	16=70%			
Late tooth eruption	4 = 25%	7=30%	0.7110	1.3125	0.3114 to 5.5317
Total	4 = 25%	23			
BW >1.5 kg					
Early tooth eruption	20 =83%	11 =92%	0.5038	0.4545	0.0450 to 4.5864
Late tooth eruption	4 =17%	1=8%			
Total	24	12			
all infants					
Early tooth eruption	32 = 80%	27=77%			0.3922 to 3.5811
Late tooth eruption	8 =20%	8=23%	0.7633	1.1852	
Total	40	35			

**Table VIII:** Impact of gestational age ; birth weight ; and gender on dentition of preterm infants.

All infants, n=110	Early tooth eruption	Late tooth eruption	p-value	Odds ratio	95% CI
Preterm GA >32 week, n=66	58	8			
Preterm G A <32 week, n=44	25	19	0.0004	5.5100	2.1312 to 14.2457
Preterm B.W >1.5kg, n=49	42	7			
Preterm B.W <1.5kg, n=61	41	20	0.0287	2.9268	1.1181 - 7.6617
Males, n=50	43	7			
Females, n=60	40	20	0.0223	3.0714	1.1732 - 8.0411

supplemented to preterm infants on the time of the first tooth eruption, our data showed that the mean of numbers of breast fed infants with early tooth eruption ( with the least content of vitamin D in milk ) was significantly more than the means of the other two groups ( $P$  - value = 0.036 ), which means that increased vitamin D content in milk or extra supplementation with oral vitamin D, has no effect on early first tooth eruption.( Table IV). At the same time the mean of numbers of infants in the three groups with late tooth eruption was not significantly different (  $P$ - value = 0.269), which means that there is no effect of vitamin D content of milk ( equal or more than breast milk) on the late tooth eruption.( Table V ).

Cross tabulation to compare the breast fed infants with different gestational ages and different birth weight with the infants in the other two groups in respect to early versus late first tooth eruption by estimation of Odds ratio, 95% CI, and  $P$ - value, we found that there was no statistically significant effect of increased vitamin D content more than in breast milk on the early versus late first tooth eruption as shown in the following Tables. (V, VI, VII)

We have compared the early and late tooth eruption according to the gestational age and birth weight of preterm infants. We have found that gestational age strongly affects the time of teething (more mature infants have higher chance for early tooth eruption than less mature ) odds ratio =5.5100 95% CI = 2.1312 - 14.14.2457 and  $p$  value =0.0004 (Table VIII ), and preterm infants with birth

weight less than 1.5 kg have more susceptibility to late tooth eruption than those with birth weight more than 1.5 kg .Odds ratio = 2.9268, 95 % CI = 1.1181 - 7.6617, and  $p$  - value = 0.0287.( Table VIII).

Finally the study data showed that females of all gestational ages and birth weight have more susceptibility to late tooth eruption than males (Odds ratio = 3.0714, 95 % CI = 1.1732 - 8.0411, and  $p$  - value = 0.0223) (Table VIII).

## Discussion

The impact of deferent neonatal factors (e.g., oral intubation, nutrition, infections, and medications) on first tooth eruption of premature infants was a prospective, longitudinal study by Rose *et al* in 1994.<sup>(15)</sup> The effect of calcium, phosphorus, and vitamin D supplementation on dental maturation in preterm infants has not been reported but only in one study by M C Backström, *et al.* ,2000,<sup>(16)</sup> but the study did not concentrate on the effect of oral vitamin D supplementation on the time of first tooth eruption in premature infants. This study is the first study to elucidate the impact of oral vitamin D supplementation on the time (early versus late chronological age) of first tooth eruption in premature infants. Our study showed that increased vitamin D content in milk or extra supplementation with oral vitamin D, had no effect on the time of the first tooth eruption of premature infants. (Table IV & V), which confirms the results of Backström, *et al* study. <sup>(16)</sup> Comparing the breast fed infants with different gestational

ages and different birth weights with the infants in the other two groups in respect to early versus late first tooth eruption, a correlations that was not studied before, our study showed that there was no statistically significant effect of increased vitamin D content more than in breast milk on the early versus late first tooth eruption of the premature infants as shown in the Tables.<sup>(5,6,7)</sup> The study showed that in general the gestational age strongly affects the time of teething (more mature infants has higher chance for early tooth eruption than less mature ) (Table VIII ), and the same effect has the birth weight as preterm infants with birth weight less than 1.5 kg have more susceptibility to late tooth eruption than those with birth weight more than 1.5 kg.( Table VIII ). These findings support previous studies (Drummond 1992, Seow1988, and Trupkin1974 ).<sup>( 8,10,12)</sup> In a study done by Viscardi and co-workers, the delay of eruption of deciduous teeth was shown in low birth weight (LBW) and premature infants .<sup>(13)</sup> Lowoyin *et al.* (1996) showed the number of erupted teeth was related to age of the infant and to some extent to weight of them.<sup>(17)</sup> Fadavi and co-workers' (1992) in a study on LBW and very Low birth weight (VLBW) infant showed that premature infants had low numbers of erupted teeth in comparison with controls.<sup>(15)</sup> Finally the study data agreed with the data of the studies conducted by Backström, *et al.*,<sup>(16)</sup> and Garn SM, *et al* <sup>(18)</sup> in that and in general females of all gestational ages and birth weight have more susceptibility to late tooth eruption than males.( Table VIII ).

## Conclusion

There is clear evidence that extra supplementation with oral vitamin D has no effect on the time of first tooth eruption of premature infants.

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