

The Role of Vitamin D and Zinc Against Oxidative Stress and Placental Senescence in Preterm Birth

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Objective

To examine the role of vitamin D and zinc against oxidative stress and placental senescence in women who underwent spontaneous preterm labor and term labor

Design

Comparative cross-section study

Methods

Maternal serum and placental samples of term labor and spontaneous preterm labor were taken during 2017-2019 in two hospitals in Jakarta, Indonesia. Markers related to metabolism of vitamin D (25OHD, 1,25OH2D3, vitamin D receptor (VDR), CYP27B1) and zinc (Zinc, ZNT1, ZIP8), oxidative stress (8-OHdG), and placental senescence (GLB1, HMGB, and telomere T/S ratio) were evaluated with enzyme-linked immunosorbent assay (ELISA), liquid chromatography–mass spectrometry (LC-MS/MS), Inductively coupled plasma mass spectrometry (ICP-MS), and polymerase chain reaction (PCR).

Table 1. Characteristics of subjects

	Normal (n=34)	Preterm (n=33)	p
Maternal age (year)	29,59 ± 5,79	27,79 ± 7,36	0,268
Gestational age (weeks)	39.44 ± 1.13	32.53 ± 2.57	<0.001
BMI (kg/m²)	23,75 (16,6-24,8)	21,70 (14,4-24,6)	0,129
History of preterm delivery			
No	32	31	0,070
Yes	2	2	
Birth weight (gram)	3176.71 ± 400.07	1884.56 ± 542.59	<0.001

Table 2. Concentrations of vitamin D, zinc, oxidative stress, and placental senescence markers in both groups

	Normal	Preterm	p
Maternal serum			
25(OH)D serum (ng/ml)	16.58±6.80	16.86±10.96	0.977
Zink serum (ug/dL)	56.29±22.97	43.45±15.45	0.009
Placenta			
25(OH)D (ng/g)	30.43±37.9	28.89±27.05	0.457
CYP27B1 (pg/mg)	7.86±3.87	7.64±3.22	0.520
1,25(OH)2D3 (pg/mg)	5.57±3.50	4.58±2.90	0.037
VDR (pg/mg)	16.48 (1.87-74.67)	21.70 (6.06-73.4)	0.041
Zinc (ug/g)	47.28±28.98	40.42±31.27	0.328
ZNT1 (pg/g)	90.22±47.27	95.35±43.32	0.560
ZIP8 (pg/mg)	4.25 (1.07-26)	3.89±4.19 (1.07-24.8)	0.736
Senescence marker			
8-OHdG (pg/mg)	0.98(0.55-9.24)	0.69(0.48-8.23)	0.144
GLB1 (pg/mg)	1568.10±759.71	1546.70±659.84	0.936
HMGB (pg/mg)	135.50±61.88	156.15±49.05	0.085
Telomere ratio T/S	1.19±0.11	1.16±0.07	0.181

Table 3. Correlation of vitamin D clusters with oxidative stress and placental senescence markers

	Placental 25(OH)D		CYP27B1		1,25(OH)2D3		VDR	
	r	p	r	p	r	p	r	p
Maternal serum								
25(OH)D	0.117	0.348	0.095	0.461	-0.062	0.623	-0.116	0.355
Placenta								
25(OH)D			-0.395	0.001	0.436	<0.001	-0.277	0.023
CYP27B1					-0.218	0.084	0.014	0.909
1,25(OH)2D3							-0.368	0.002

Table 4. Correlation of zinc clusters with oxidative stress and placental senescence markers

	Placental Zinc		ZNT1		ZIP8	
	r	p	r	p	r	p
Maternal serum						
Zinc	-0.156	0.207	0.405	<0.001	0.311	0.010
Placenta						
Zinc			-0.179	0.144	-0.071	0.564
ZNT1					0.471	<0.001

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Table 5. Correlation of vitamin D and zinc clusters with oxidative stress and placental senescence markers

	8-OHdG		GLB1		HMGB1		Telomere Ratio	
	r	p	r	p	r	p	r	p
Placenta								
25(OH)D	-0.235	0.055	-0.337	0.005	-0.149	0.228	-0.252	0.040
CYP27B1	0.256	0.048	0.585	<0.001	0.373	0.003	0.340	0.008
1,25(OH)2D3	-0.297	0.014	-0.374	0.002	-0.289	0.017	-0.014	0.913
VDR	-0.046	0.711	0.457	<0.001	0.134	0.277	-0.059	0.635
Zinc	0.115	0.352	-0.053	0.666	0.035	0.777	0.130	0.293
ZNT1	0.1182	0.138	0.689	<0.001	0.252	0.038	0.051	0.680
ZIP8	0.531	<0.001	0.433	<0.001	0.211	0.084	-0.063	0.614

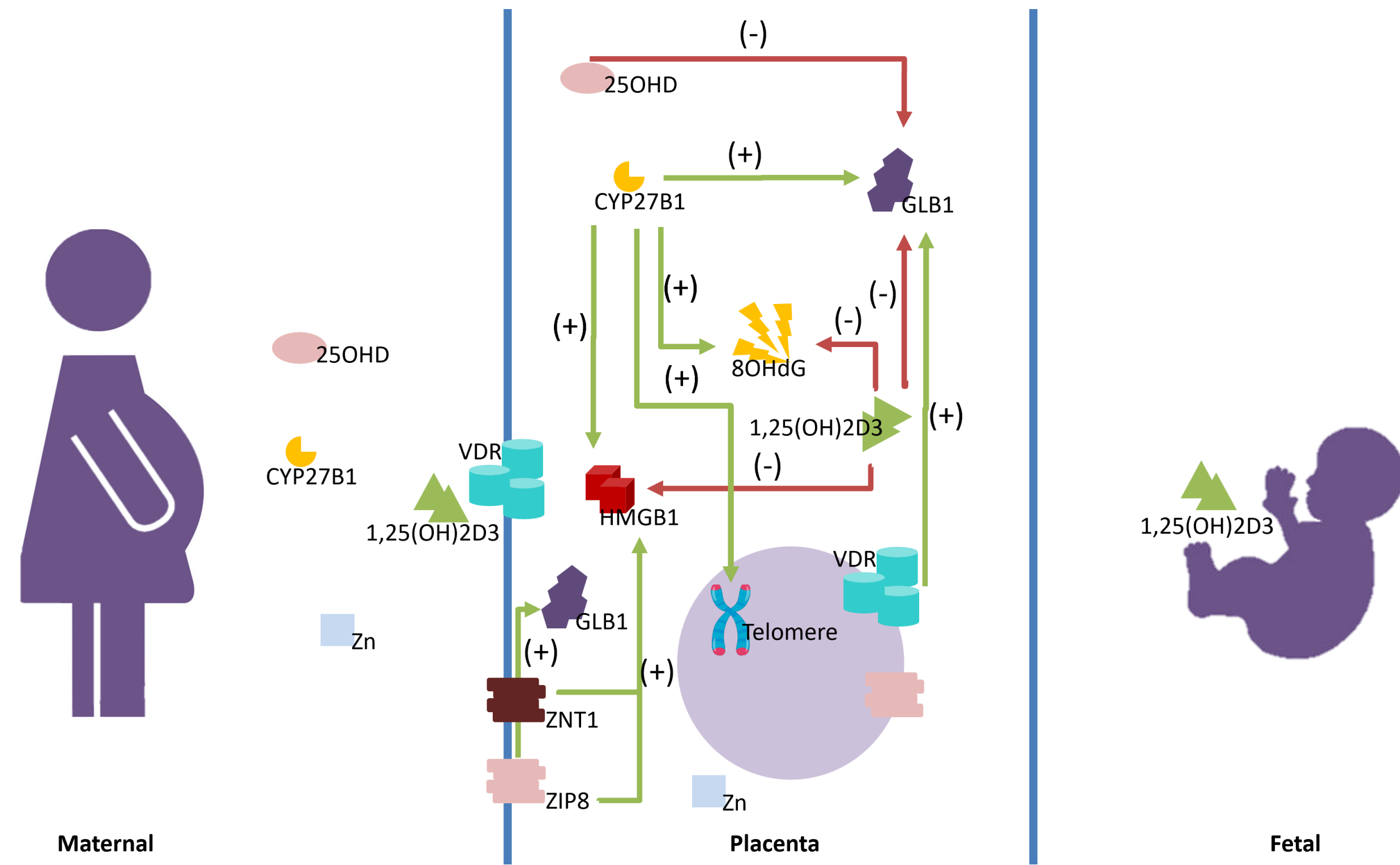


Figure 1. Proposed mechanism of protective factor of vitamin D and zinc against placental senescence

Conclusion

Malnutrition, particularly micronutrient deficiency, remains a challenge. Its deficiency might contribute to the pathophysiology of placental oxidative stress and senescence that leads to preterm birth, as this study showed the correlation between placental vitamin D and zinc with oxidative stress and senescence markers. The correlation between placental vitamin D receptor, vitamin D enzyme, and zinc transporters with the oxidative stress and senescence markers suggest an immaculate regulation to meet the required substance, albeit maternal deficiency.