Vitamin D deficiency in pregnancy associates with increased emotional and behavioral problems at preschool age: the Rhea pregnancy cohort, Crete, Greece

Vasiliki Daraki[1, 2], Theano Roumeliotaki[1], Georgia Chalkiadaki[1], Andrew Margioris[3], Katerina Koutra[1], Marianna Katrinaki[3], Andriani Kyriklaki[1], Mariza Kampouri[1], Stathis Papavasiliou[2], Manolis Kogevinas[4], Leda Chatzi[1]

[1]Department of Social Medicine, Faculty of Medicine, University of Crete, Heraklion, Greece, [2]Department of Endocrinology, Diabetes and Metabolic Diseases, University Hospital of Crete, Heraklion, Greece, , [3]Lab of Clinical Chemistry-Biochemistry, Department of Laboratory Medicine, School of Medicine, University of Crete, Heraklion, Greece, [4]National School of Public Health, Athens, Greece

BACKGROUND

Vitamin D deficiency is now recognized as a worldwide pandemic[1] even in countries with abundant sunshine[2] like Greece[3].

Recent epidemiological data indicate high prevalence of vitamin D deficiency in pregnant women and their infants[4], whose vitamin D levels are largely dependent on their mothers' status.

Vitamin D during pregnancy is playing an important role in fetal brain development, as it regulates proliferation and differentiation of brain cells, and has neurotrophic and neuroprotective actions[5] .

Animal studies support an association beytween low maternal vitamin D levels during pregnancy and offspring longer brains[6], with increased ventricular volume and a thinner neocortex as well as abnormal behaviors in adulthood[7].

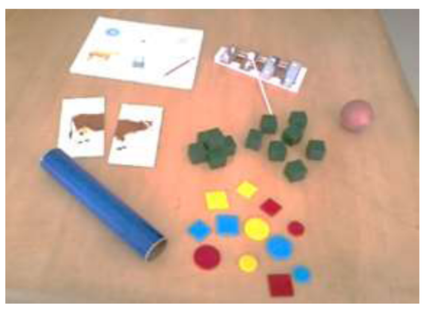
However data in humans is scarce with conflictive results[8,9,10].

OBJECTIVES

To investigate the associations of maternal 25-hydroxyvitamin D [25(OH)D] levels in early pregnancy with offspring neurodevelopment at 4 years of age, using data from a longitudinal, prospective pregnancy cohort, "Rhea" study in Crete, Greece.

METHODS

471 mother-child pairs were included in the present analyses



Exposure assessment:

Maternal plasma concentration of 25(OH)D at the first prenatal visit (13±2.4 weeks).

According to Endocrine society association (2011) maternal 25(OH)D was categorized as:

sufficiency (>75nmol/l), insufficiency (52.5-72.5nmol/l) and deficiency(50nmol/l)

Outcome assessment:

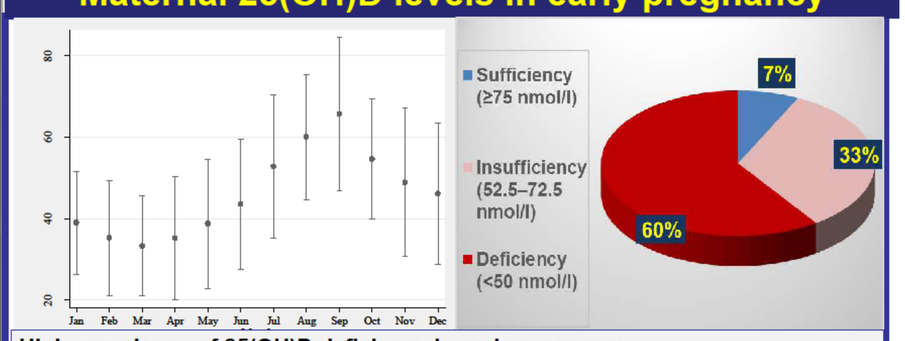
- ✓ Offspring cognitive and motor function at 4 years of age was assessed by means of McCarthy Scales of Children's Abilities (MSCA), which contains six scales: Verbal, Perceptual-Performance, Quantitative, General Cognitive, Memory and Motor scale.
- ✓ Emotional and behavioral development at 4 years was assessed by means of Strengths and Difficulties Questionnaire (SDQ) and Attention Deficit Hyperactivity Disorder (ADHD) Test.

Data analysis:

Multivariable linear regression models were used to estimate the effect of maternal vitamin 25(OH)D in early pregnancy on child neurodevelopment at 4 years of age after adjusting for multiple confounders.

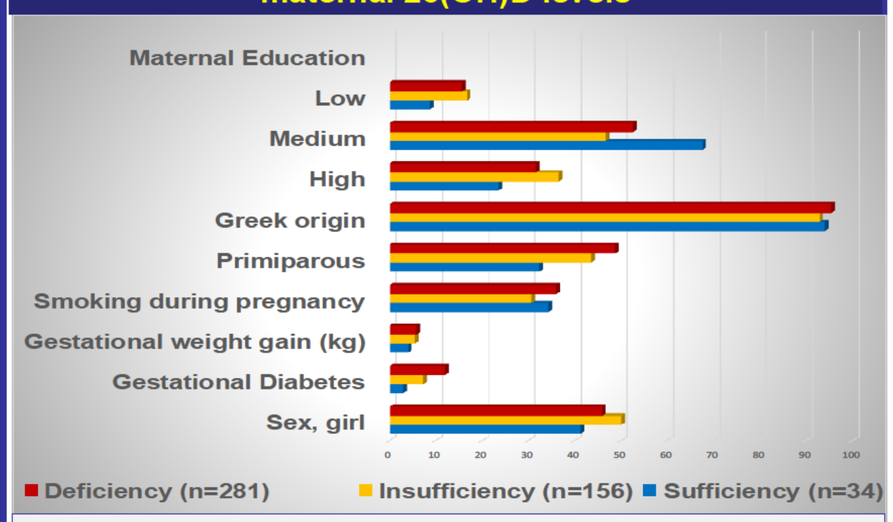
RESULTS

Maternal 25(OH)D levels in early pregnancy



High prevalence of 25(OH)D deficiency in early pregnancy

Descriptive characteristics of the study population by maternal 25(OH)D levels



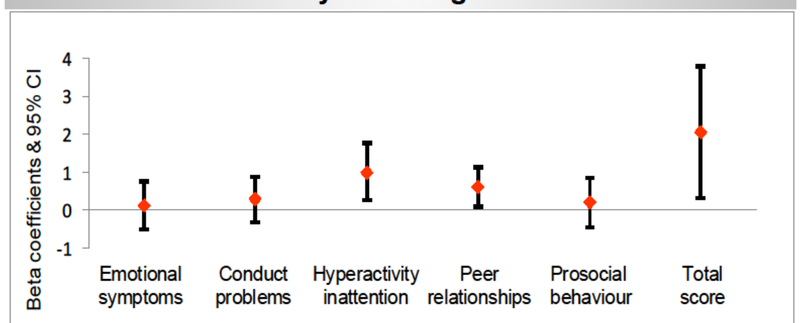
Maternal 25(OH)D levels in early pregnancy were not associated with maternal sociodemographic characteristics

Maternal 25(OH)D deficiency in early pregnancy was associated with increased:

- ➢ **Child hyperactivity/inattention symptoms** (b-coef 0.58, 95%CI: 0.03, 1.12)
- ➢ **Child peer relationship problems** (b-coef: 1.15, 95%CI: 0.36, 1.94)
- ➢ **Child total strengths and difficulties score** (b-coef: 2.07, 95%CI: 0.25, 3.89)
- ➢ **Child total ADHD-like symptoms** (b-coef: 5.36, 95%CI: 0.75, 9.98)

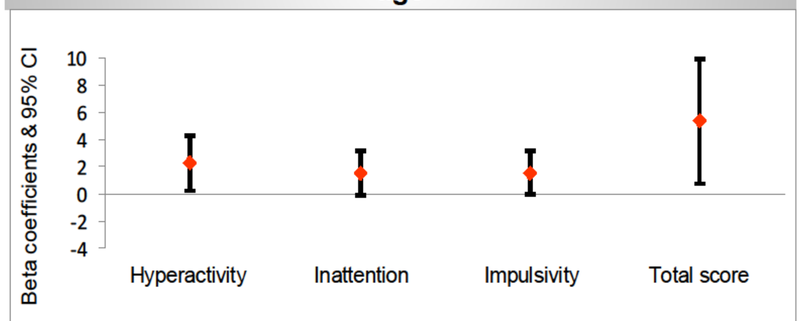
No significant association was found between maternal 25(OH)D deficiency in early pregnancy and cognitive and motor function at 4 years of age

Association between maternal 25 (OH)D deficiency in early pregnancy and strengths and difficulties(SDQ) at 4 years of age



All models were adjusted for child sex, child age of assessment, month of maternal vitamin D sampling. maternal age, maternal education, parity and maternal body mass index pre-pregnancy

Association between maternal 25 (OH)D deficiency in early pregnancy and ADHD –like symptoms at 4 years of age



All models were adjusted for child sex, child age of assessment, month of maternal vitamin D sampling. maternal age, maternal education, parity and maternal body mass index pre-pregnancy

CONCLUSIONS

Vitamin D deficiency in early pregnancy was associated with increased emotional and behavioral problems at preschool age. Further research is needed to replicate these results and to explore potential underlying biological mechanisms.

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