

Vitamin B12 and folic acid status of term pregnant women and newborns in the Antwerp region, Belgium

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Summary

Objective: Descriptive study on maternal serum vitamin B12 and folic acid in term pregnancy and in umbilical cord blood that was performed in an inner city hospital with a mixed ethnic population in the region of Flanders in Belgium. **Materials and Methods:** A prospective cohort study that took place from April 1 until May 31, 2011. Plasma folic acid and vitamin B12 were measured in maternal and umbilical cord blood from all term uncomplicated deliveries in a single regional hospital. Data on age, previous obstetric history, ethnicity, nutritional intake, and use of vitamin supplements were registered. **Results:** Data were collected from 110 patients, mean maternal serum vitamin B12 was 243.9 pmol/l and mean folic acid level was 43.0 nmol/l. Using a cutoff of respectively 150 pmol/l for vitamin B12 and 7.1 nmol/l for folic acid, 13% of the women were classified as vitamin B12-deficient and 23% were deficient for folic acid. Vitamin B12 deficiency was only seen in autochthonous Belgian women. A correlation between the maternal and umbilical cord levels was noted ($R = 0.7$ for vitamin B12, $R = 0.85$ for folic acid), but none of the umbilical cord levels demonstrated deficiency. Number of previous pregnancies and intake of supplements had no influence. **Conclusion:** Pregnant women in Antwerp, Belgium, frequently show vitamin B12 and folic acid deficiency, although a correlation exists with lower umbilical cord levels, the present limited data did not demonstrate any case of deficiency in umbilical cord blood. The frequency is highest in the autochthonous population and is not influenced by intake of vitamin supplements.

Key words: Vitamin B12; Cobalamin; Pregnancy; Umbilical cord; Vitamins; Ethnicity; Folic acid.

Introduction

Vitamin B12 or cobalamin is a co-enzyme in folate metabolism which is crucial to cell multiplication in pregnancy. The rapidly dividing placental and fetal tissue result in an increased need for both cobalamin and folic acid in pregnancy. Although much has been written on the role of folic acid supplementation in the periconceptional period and the prevention of neural tube defects, much less is known on the effects later in pregnancy. There are no clear cut reference values for vitamin B12 status in pregnant women; it has been suggested that serum vitamin B12 should be at least 221 to 295 pmol/l and the levels have been shown to differ between racial/ethnic groups [1-3].

In this study we aim to describe the cobalamin and folate level in maternal serum and umbilical cord in uncomplicated term pregnant women in an ethnically mixed city population in western Europe.

Materials and Methods

This was a descriptive single center study performed at Antwerp University Hospital (Edegem, Belgium). From April 1 to May 31, 2011, all term pregnant women presenting with spontaneous term labour were asked to have a blood sample drawn for vitamin B12 and folic acid, both a venous maternal serum sample immediately after informed consent was obtained and a sample from the umbilical vein at delivery. The study was ap-

proved by the local ethics committee and all patients signed a written informed consent. Term pregnancy was defined as 37 weeks or later, and complications such as diabetes, hypertension, fetal growth retardation or any other maternal disorder necessitating special care during pregnancy (including bariatric surgery and a previous baby with a congenital malformation), were excluded. A short food questionnaire was presented including questions on previous pregnancy and delivery, birth weight of previous children, previous surgery, congenital anomalies in the family (specifically asking for neural tube defects), use of vitamin supplements during pregnancy, any medication, eating eggs, meat, fish, vegetables, fruits, and alcoholic beverage consumption. Patients were also asked for their self-identified ethnic group; possibilities included autochthonous Belgian, Moroccan, Turkish, Central African, Western European (other than Belgian), Asian and "other".

Vitamin B12 was analysed and folic acid in maternal serum was measured. A serum level below 150 pmol/l was considered vitamin B12 deficiency; lower than 7.1 nmol/l was defined as folic acid deficiency, both as defined by WHO [4].

Statistics were performed with the SPSS 20.0 package. The authors used mean, standard deviation, differences between groups were compared with Student's t- test, and significance accepted at $p < 0.05$. Spearman correlation analysis was used to check for correlation between maternal and umbilical cord values. Linear regression was performed to evaluate other factors such as nutrition and use of supplements.

Results

Of 110 women included in the study period, 90 (81.8%) completed the questionnaire. There were 54 (48.8%) primiparous and 56 (51.2%) multiparous women. Eighty-three women (75.6%) were using vitamin supplements.

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An only brand was used containing 2.7 micrograms of vitamin B12 and 800 micrograms of L-methyl folic acid. There were 56 (51%) autochthonous Belgian women, 26 (24%) Moroccan, eight (7%) Asian, eight (7%) Central African, ten (9%) Western European other than Belgian, and only two (2%) Turkish.

Maternal serum vitamin B12 and folic acid were available for 78 (71%) of women, patients with missing samples were almost all women having signed the informed consent, but delivery was completed before blood samples were taken, mainly during night time. Mean serum cyanocobalamin was 243.9 pmol/l (standard deviation 93.9 pmol/l, minimum 2 pmol/l, maximum 500 pmol/l), mean folic acid in maternal serum was 43.0 nmol/l (standard deviation 185.2 nmol/l); this extremely large standard deviation was due to one woman having an extremely high level (1,168 nmol/l), excluding this outlier from further analysis led to a mean value of 13.5 nmol/l (standard deviation 12.9 nmol/l, minimum 2.9 nmol/l, and maximum 21 nmol/l). Vitamin B12 deficiency was noted in ten (13% of serum samples) women; folic acid deficiency in 18 (23% of serum samples); none of these women had hemoglobin < 10.5 gram/dl. All cases of vitamin B12 deficiency were autochthonous Belgian women. Twelve out of 18 (66.7%) cases with folic acid deficiency were also autochthonous Belgian.

Umbilical cord blood samples were available for 88 cases (80%). Mean serum vitamin B12 was 612.7 pmol/l (standard deviation 414.0 pmol/l, maximum 1,586 pmol/l, and minimum 172 pmol/l); mean serum folic acid on umbilical cord venous blood was 18.4 nmol/l (standard deviation 3.7 nmol/l, maximum 21 nmol/l, and minimum eight nmol/l). Correlation between maternal and umbilical cord levels was rather weak (Spearman correlation coefficient $R = 0.7$) for cobalamin, and strong for folic acid ($R = 0.85$). There were no umbilical cord samples below the cut-off for deficiency, neither for vitamin B12 or folic acid.

Significant factors in linear regression determining maternal serum levels for folic acid were not eating eggs ($p = 0.001$) and consuming alcohol at least three to four times weekly ($p = 0.001$). For vitamin B12, alcohol consumption also was significant ($p = 0.033$), but no other factors reached significance. Using a vitamin supplement was not related to the maternal serum level of vitamin B12 nor to folic acid.

Discussion

Despite the fact that the majority of women in the present sample was using vitamin supplementation, deficiencies for both folic acid and vitamin B12 were frequent and not less so in those using vitamin preparations containing folic acid and cobalamin. This can both be due to biologic factors, such as interference with food or ab-

sorption, but it can also be due to bias in reporting: perhaps women who report using vitamins do not really take them.

Reduced folate and increased vitamin B12 have been related to preterm birth and intrauterine growth restriction [5,6]; the present data demonstrate that folate and vitamin B12 deficiency are very frequent in normal term pregnancies (none of the babies in this cohort had a birth weight below 2,700 grams, the fifth percentile in this population), and considerable variation exists in these normal term pregnant women. A physiologic gradual decline in the serum concentration of vitamin B12, reaching a minimum at 32 weeks and the progressively rising again to term has been found by Morkbak *et al.* [7], as a high maternal serum concentration of vitamin B12 seems to be related to more preterm delivery and fetal growth impairment supplementation, with higher doses than in the kind of preparation used by the present patients might be harmful. There were no cases of low values for folate or vitamin B12 in umbilical cord (i.e. fetal) serum, underlining the inaccuracy of maternal serum levels to predict any deficiency in the offspring.

No clinically validated normal values for vitamin B12 or folate in pregnancy, including cut off values necessitating supplementation have been published. The present data suggest that cut-off values such as used in the non-pregnant population should not be used as far as provision of factors to the fetus is concerned, despite the correlation between maternal and umbilical cord levels; the latter were always above the minimal required level, suggesting a fetal benefit in supply even in case of maternal deficiency.

The present data do not allow any comment on the relation with neural tube defects or any other complication of pregnancy as the authors include only normal term pregnancies and not early pregnancy.

The autochthonous Belgian population has the highest risk for deficiencies in both vitamin B12 and folic acid. This can be partly explained by alcohol consumption (none of the Moroccan women consumed alcohol); this is just one more argument against the use of alcohol in pregnancy. The authors can only hypothesize that differences in diet are responsible for this and the food questionnaire utilized in the present cohort was not detailed enough to reveal this.

Conclusion

Pregnant women in Antwerp, Belgium, frequently show vitamin B12 and folic acid deficiency, correlated to lower umbilical cord levels but not as strong to lead to insufficient levels in umbilical/fetal blood. The frequency is highest in the autochthonous population and is not influenced by intake of vitamin supplements, but is associated to alcohol use.

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