



West Middlesex University Hospital

Vitamin B12 deficiency in pregnancy

Date of Search: 13/06/2016

Sources Searched: Medline, Embase, DynaMed, NHS Evidence Search, CKS.

Summary:

There is currently no standard test for measuring vitamin B12 deficiency. Recent guidelines for the diagnosis and treatment of cobalamin and folate disorders from the British Society for Haematology (Devalia et al. 2014 attached) state that serum total vitamin B12 remains the first-line test because of its wide availability and low cost, but that it lacks the sensitivity and specificity needed for a robust diagnostic test. Plasma methylmalonic acid testing is used to clarify uncertain results, however this may be falsely elevated in people with renal disease, haemoconcentration or small bowel bacterial overgrowth and the high cost of the test has prevented its widespread use (Devalia et al. 2014). The guidelines state that serum holoTC has the potential to be used as a first-line test and may reduce the number of indeterminate results, particularly in people over 65 years. They further state that holoTC has the added advantage that it can be used in **pregnant women** and in women taking oral contraceptives, because the holoTC fraction of cobalamin does not seem to have the same physiological reduction over the course of pregnancy as total serum cobalamin. These guidelines state that further studies are needed to evaluate the clinical utility of holoTC in assessing vitamin B12 deficiency in a routine high-output laboratory setting.

Source: NICE Active B12 assay for diagnosing vitamin B12 deficiency (Sep 2015)

<https://www.nice.org.uk/guidance/mib40/resources/active-b12-assay-for-diagnosing-vitamin-b12-deficiency-63499159342789> [Last accessed 13/06/2016]

Search History:

1. EMBASE; *CYANOCOBALAMIN DEFICIENCY/; 3326 results.
2. EMBASE; (hypocobalaminemia OR "B12 deficienc*").ti; 1630 results.
3. EMBASE; 1 OR 2; 3710 results.
4. EMBASE; pregn*.ti; 224466 results.
5. EMBASE; 3 AND 4; 59 results.
6. EMBASE; (CYANOCOBALAMIN OR B12).ti; 10699 results.
7. EMBASE; 4 AND 6; 206 results.
8. EMBASE; 5 OR 7; 226 results.
9. EMBASE; exp PREGNANCY/; 618371 results.
10. EMBASE; 3 AND 9; 157 results.
11. EMBASE; 10 [Limit to: (Publication Types Review)]; 18 results.
12. EMBASE; 6 AND 9; 406 results.
13. EMBASE; 12 [Limit to: (Publication Types Review)]; 25 results.
14. EMBASE; exp PREGNANCY COMPLICATION/; 115533 results.
15. EMBASE; 3 AND 14; 36 results.
16. EMBASE; exp REFERENCE VALUE/; 57875 results.
17. EMBASE; 12 AND 16; 7 results.
18. Medline; (hypocobalaminemia OR "B12 deficienc*" OR CYANOCOBALAMIN).ti; 1659 results.
19. Medline; pregn*.ti; 193770 results.
20. Medline; 18 AND 19; 18 results.
21. Medline; exp VITAMIN B 12 DEFICIENCY/; 10452 results.
22. Medline; 19 AND 21; 169 results.
23. Medline; (maternal OR newborn).ti; 110914 results.
24. Medline; 21 AND 23; 67 results.
25. Medline; exp FETUS/; 145830 results.
26. Medline; 21 AND 25; 29 results.
27. Medline; 18 AND 23; 20 results.
28. EMBASE; (maternal OR newborn).ti; 118812 results.
29. EMBASE; 1 AND 28; 48 results.

30. EMBASE; exp FETUS/; 160340 results.
 31. EMBASE; 1 AND 30; 10 results.
 32. Medline; exp REFERENCE VALUES/; 148594 results.
 33. Medline; 21 AND 32; 116 results.
 34. Medline; pregn*.af; 871046 results.
 35. Medline; pregn*.af; 871046 results.
 36. Medline; 33 AND 34; 8 results.
 37. EMBASE; exp FETUS GROWTH/; 11493 results.
 38. EMBASE; 1 AND 37; 3 results.
 39. EMBASE; 1 AND 37; 3 results.
 40. Medline; exp FETAL DEVELOPMENT/; 79206 results.
 41. Medline; 21 AND 40; 18 results.
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Title: Prevalence of Vitamin B-12 insufficiency during pregnancy and its effect on offspring birth weight: A systematic review and meta-analysis

Citation: American Journal of Clinical Nutrition, May 2016, vol./is. 103/5(1232-1251), 0002-9165;1938-3207 (01 May 2016)

Author(s): Sukumar N., Rafnsson S.B., Kandala N.-B., Bhopal R., Yajnik C.S., Saravanan P.

Language: English

Abstract: Background: Vitamin B-12 and folate are micronutrients essential for normal embryogenesis. Vitamin B-12 insufficiency in pregnancy is high in certain parts of the world, such as India, and although this has been linked to low birth weight (LBW) in these populations, the relation between Vitamin B-12 and birth weight (BW) elsewhere is unknown. Objectives: We performed a systematic review to assess 1) the worldwide prevalence of Vitamin B-12 insufficiency in pregnancy and 2) its association with BW. Design: A search of 5 electronic databases was performed to identify eligible articles. Random-effects meta-analysis was conducted according to geographic regions and pregnancy trimesters for the prevalence subreview and by categorical measures of BW. Results: A total of 57 and 23 articles were included for the prevalence and BW subreviews, respectively. The pooled estimates of Vitamin B-12 insufficiency were 21%, 19%, and 29% in the first, second, and third trimesters, respectively, with high rates for the Indian subcontinent and the Eastern Mediterranean. The large heterogeneity between studies was partially addressed by creating a standardized score for each study (mean Vitamin B-12 insufficiency O cutoff value), which internally corrected for geographic region, trimester, and assay type. Twelve of the 13 longitudinal studies included showed a decrease in mean or median Vitamin B-12 across trimesters. Pooled analysis showed nonsignificantly lower maternal Vitamin B-12 concentrations in LBW than in normal-BW infants and higher odds of LBW with lower Vitamin B-12 values (adjusted OR: 1.70; 95% CI: 1.16, 2.50), but studies from India largely contributed to the latter. Conclusions: Our review indicates that Vitamin B-12 insufficiency during pregnancy is common even in nonvegetarian populations and that concentrations of Vitamin B-12 decrease from the first to the third trimester. There is no consistent

association between Vitamin B-12 insufficiency and LBW. However, given the long-term risks of LBW, this observation warrants further cohort studies and randomized controlled trials.

Publication Type: Journal: Article

Source: EMBASE

Title: Vitamin B12 and folate status in early pregnancy and cardiometabolic risk factors in the offspring at age 5-6 years: findings from the ABCD multi-ethnic birth cohort.

Citation: BJOG : an international journal of obstetrics and gynaecology, Feb 2016, vol. 123, no. 3, p. 384-392, 1471-0528 (February 2016)

Author(s): Krikke, G G, Grooten, I J, Vrijkotte, T G M, van Eijsden, M, Roseboom, T J, Painter, R C

Abstract: To explore whether maternal vitamin B12 and folate status during early pregnancy are associated with cardiometabolic risk factors in the offspring at age 5-6. Prospective multi-ethnic birth cohort, the Amsterdam Born Children and their Development study (ABCD). 12,373 pregnant women living in Amsterdam were approached between 2003 and 2004 for participation in the study. Mother-child pairs for whom information on maternal vitamin B12 or folate status in early gestation and health at age 5-6 years was available (n = 1950). Vitamin B12 and folate concentrations were determined in maternal serum at intake in early pregnancy (median 13 weeks' gestation). Anthropometric measurements, blood pressure and fasting blood samples were collected during a health check of children aged 5-6 years. Multiple linear regression was performed to investigate the association between maternal serum concentrations and children's outcomes, corrected for confounders. Gestational age at birth, birthweight, body mass index (BMI), glucose levels, triglyceride levels, blood pressure and heart rate of the offspring at age 5-6. Low maternal folate levels during early pregnancy were associated with slightly higher BMI in the offspring [decrease per 10 units: β 0.07 kg/m², 95% confidence interval (CI) 0.01, 0.13]. Low maternal vitamin B12 concentrations were associated with higher heart rates (decrease per 100 units: β 0.49 beats/min, 95% CI 0.11, 0.87). This study provides further evidence that maternal nutrition in early pregnancy may possibly program cardiometabolic health of the offspring. Low folate and vitamin B12 levels during pregnancy are associated with higher BMI and heart rate in offspring. © 2015 Royal College of Obstetricians and Gynaecologists.

Source: Medline

Full Text:

Available from Wiley in [BJOG: An International Journal of Obstetrics and Gynaecology](#)

Title: Maternal micronutrient deficiencies and related adverse neonatal outcomes after bariatric surgery: a systematic review.

Citation: Advances in nutrition (Bethesda, Md.), Jul 2015, vol. 6, no. 4, p. 420-429, 2156-5376 (July 2015)

Author(s): Jans, Goele, Matthys, Christophe, Bogaerts, Annick, Lannoo, Matthias, Verhaeghe, Johan, Van der Schueren, Bart, Devlieger, Roland

Abstract: Pregnant and postpartum women with a history of bariatric surgery are at risk of micronutrient deficiencies as a result of the combination of physiologic changes related to pregnancy and iatrogenic postoperative alterations in the absorption and metabolism of crucial nutrients. This systematic review investigates micronutrient deficiencies and related adverse clinical outcomes in pregnant and postpartum women after bariatric surgery. A systematic approach involving critical appraisal was conducted independently by 2 researchers to examine deficiencies of phyloquinone, folate, iron, calcium, zinc, magnesium, iodide, copper, and vitamins A, D, and B-12 in pregnant and postpartum women after bariatric surgery, together with subsequent outcomes in the neonates. The search identified 29 relevant cases and 8 cohort studies. The quality of reporting among the case reports was weak according to the criteria based on the CARE (CAse REporting) guidelines as was that for the cohort studies based on the criteria from the Cohort Study Quality Assessment list of the Dutch Cochrane Center. The most common adverse neonatal outcomes related to maternal micronutrient deficiencies include visual complications (vitamin A), intracranial hemorrhage (phyloquinone), neurological and developmental impairment (vitamin B-12), and neural tube defects (folate). On the basis of the systematically collected information, we conclude that the evidence on micronutrient deficiencies in pregnant and postpartum women after bariatric surgery and subsequent adverse neonatal outcomes remains weak and inconclusive. © 2015 American Society for Nutrition.

Source: Medline

Title: Maternal adiposity is associated with lower maternal vitamin B12 and folate in pregnancy

Citation: BJOG: An International Journal of Obstetrics and Gynaecology, April 2015, vol./is. 122/(259-260), 1470-0328 (April 2015)

Author(s): Knight B., Shields B., Brook A., Yajnik C., Hattersley A.T.

Language: English

Abstract: Introduction Vitamin B12 and folate are essential micronutrients, which support the increased metabolic demands of pregnancy. Previous studies of pregnant women in India describe an association of maternal adiposity with vitamin B12 deficiency in a population where nutrient deficiency is common. We explored whether the same associations exist in a non-diabetic Caucasian pregnant cohort. Methods We utilised the Exeter Family Study of Child Health (EFSOCH) dataset, an extensively characterised UK pregnancy cohort (n = 995) for which routine anthropometric and biochemical measurements are available. Vitamin B12 and folate were measured at 28 weeks (+/- 5 days) by microbiological assay at the KEM Hospital, Pune, India. Data was available on 28 week maternal body mass index (BMI), sum of skinfold thickness (SSFT), insulin resistance (IR) and triglycerides in addition to pregnancy and lifestyle factors. Maternal aspartate transaminase (AST) and alanine aminotransferase (ALT) activity were also measured at 28 weeks. Descriptive statistics are median and interquartile range (IQR) and non-normally distributed values were log transformed for correlation and multivariate regression analysis. Results There was a negative association of BMI (26.9 IQR 5.52) with both vitamin B12 (201 pg/L IQR 104) and folate (13.8 nmol/L IQR 14; R = -0.271 and -0.150; P < 0.00 respectively). For vitamin B12 this observation extended to other adiposity surrogates such as maternal SSFT (52.3 IQR 26.7; R = -0.269; P < 0.00), IR (0.125 IQR 0.01; R = -0.234; P < 0.00) and triglycerides (2.00 IQR 0.91; R = -0.217; P < 0.00). 198 mothers (20%) had vitamin B12 < 150 pmol/L indicating true vitamin B12 deficiency and these women had significantly higher BMI (29.3 versus 26.6; Mann-Whitney P < 0.00). Multivariate regression analysis controlling for age, parity, vitamin supplementation, vegetarianism, social class and haemodilution revealed that for

every one unit increase in BMI, there was a corresponding decrease of 0.4% in vitamin B12 and 0.3% in folate ($P < 0.00$ for both). Vitamin B12 correlated positively with both AST and ALT independent of IR ($R = 0.283$ and 0.235 respectively; $P < 0.00$). A similar relationship was observed between folate, AST and ALT ($R = 0.224$ and 0.169 respectively; $P < 0.00$). Conclusion Maternal adiposity was associated with both lower vitamin B12 and folate in this Western pregnancy cohort. These findings are important for understanding the effect of adipose in pregnancy on the circulating maternal micronutrient reservoir. The positive associations of vitamin B12 and folate with liver transaminases warrant further study as they are not explained simply by insulin resistance but alternatively could indicate altered micronutrient turnover or hepatic storage in these pregnancies.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:

Available from *Wiley* in [BJOG: An International Journal of Obstetrics and Gynaecology](#)

Title: Low vitamin B12 in pregnancy is associated with maternal obesity and gestational diabetes

Citation: Diabetic Medicine, March 2015, vol./is. 32/(79-80), 0742-3071 (March 2015)

Author(s): Sukumar N., Wilson S., Venkataraman H., Saravanan P.

Language: English

Abstract: Aims: Vitamin B12 insufficiency has been linked with adiposity and insulin resistance. A study from India showed that B12 insufficiency in pregnancy was associated with higher risk of gestational diabetes (GDM), mediated by body mass index (BMI). It is not known whether the same association exists among pregnant women in the UK. Methods: A retrospective study was done on women attending our antenatal clinic from 2010 to 2013. Information including maternal demographics, first trimester BMI, B12, folate and glucose were collected and multivariate regression models were applied. Results: 247 women (114 GDM, 133 controls) who had B12 levels checked in early third trimester were included. Overall, 26.7% had B12 values <150 pmol/l. GDM mothers were older and more obese than controls and had significantly lower mean B12 (186 vs 225 pmol/l, $p = 0.01$) with similar folate levels. In all women, first trimester BMI had a significant negative correlation with third trimester B12 ($r = -0.203$, $p = 0.001$). Linear regression showed that BMI was the only significant predictor of B12 ($\beta = -0.21$, $p = 0.002$), after adjusting for age, parity, ethnicity and folate. Women in the lowest B12 tertile had significantly higher odds of a diagnosis of GDM than those in the highest tertile (adjusted odds ratio 2.27, 95% confidence interval 1.07, 4.78), after adjusting for BMI and other variables as above. Conclusion: This study shows, for the first time in a UK population, that obese pregnant women in the UK are at risk of B12 insufficiency in pregnancy, which in turn is independently associated with GDM. Further studies are urgently needed to explore this link.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:

Available from *Wiley* in [Diabetic Medicine](#)

Title: Relationships of maternal folate and vitamin B12 status during pregnancy with perinatal depression: The GUSTO study

Citation: Journal of psychiatric research, August 2014, vol./is. 55/(110-116), 1879-1379 (01 Aug 2014)

Author(s): Chong M.F., Wong J.X., Colega M., Chen L.-W., van Dam R.M., Tan C.S., Lim A.L., Cai S., Broekman B.F., Lee Y.S., Saw S.M., Kwek K., Godfrey K.M., Chong Y.S., Gluckman P., Meaney M.J., Chen H.

Language: English

Abstract: UNLABELLED: Studies in the general population have proposed links between nutrition and depression, but less is known about the perinatal period. Depletion of nutrient reserves throughout pregnancy and delayed postpartum repletion could increase the risk of perinatal depression. We examined the relationships of plasma folate and vitamin B12 concentrations during pregnancy with perinatal depression. At 26th-28th weeks of gestation, plasma folate and vitamin B12 were measured in women from the GUSTO mother-offspring cohort study in Singapore. Depressive symptoms were measured with the Edinburgh Postnatal Depression Scale (EPDS) during the same period and at 3-month postpartum. EPDS scores of >15 during pregnancy or >13 at postpartum were indicative of probable depression. Of 709 women, 7.2% (n = 51) were identified with probable antenatal depression and 10.4% (n = 74) with probable postnatal depression. Plasma folate concentrations were significantly lower in those with probable antenatal depression than those without (mean +/- SD; 27.3 +/- 13.8 vs 40.4 +/- 36.5 nmol/L; p = 0.011). No difference in folate concentrations was observed in those with and without probable postnatal depression. In adjusted regression models, the likelihood of probable antenatal depression decreases by 0.69 for every unit variation (increase) in folate (OR = 0.69 per SD increase in folate; 95% CI: 0.52, 0.94). Plasma vitamin B12 concentrations were not associated with perinatal depression. Lower plasma folate status during pregnancy was associated with antenatal depression, but not with postnatal depression. Replication in other studies is needed to determine the direction of causality between low folate and antenatal depression. CLINICAL TRIAL REGISTRY: NCT01174875.

Publication Type: Journal: Article

Source: EMBASE

Title: Serum vitamin B12 levels during the first trimester of pregnancy correlate with newborn screening markers of vitamin B12 deficiency

Citation: International journal for vitamin and nutrition research. Internationale Zeitschrift für Vitamin- und Ernährungsforschung. Journal international de vitaminologie et de nutrition, 2014, vol./is. 84/1-2(92-97), 0300-9831 (2014)

Author(s): Dayaldasani A., Ruiz-Escalera J., Rodriguez-Espinosa M., Rueda I., Perez-Valero V., Yahyaoui R.

Language: English

Abstract: INTRODUCTION: Low maternal vitamin B12 status is a risk factor for various adverse pregnancy outcomes. Although vitamin B12 deficiency is not a primary target of newborn screening (NBS) programs, measurements of propionylcarnitine (C3) and its ratios with acetylcarnitine (C3/C2) and palmitoylcarnitine (C3/C16) may incidentally identify vitamin B12-deficient newborns. The objective of this study was to measure vitamin B12 levels in women during the first trimester of pregnancy, evaluate predictors of these concentrations, and study their relationship with newborn screening results. DESIGN: Vitamin B12 concentrations were evaluated in 204 women during the first trimester of pregnancy and possible confounding factors were analyzed. After giving birth, data of their newborns (189) were collected (sex, gestational age, birthweight) and the acylcarnitine profile obtained by tandem mass spectrometry during NBS was analyzed. To assess the effects of the variables on vitamin B12 serum concentrations and newborn screening markers, stepwise multiple linear regression models were used. RESULTS: The mean serum concentration of vitamin B12 was 370.8 pmol/L (502.4 pg/mL) (SD 142.81). Vitamin B12 concentrations were significantly lower in smokers ($p=0.027$), and in women with low meat consumption ($p=0.040$). There was a significant inverse correlation between mothers' vitamin B12 concentrations and their children's C3 ($r=-0.24$; $p=0.001$), C3/C2 ($r=-0.23$; $p=0.002$) and C3/C16 levels ($r=-0.20$; $p=0.006$). CONCLUSIONS: Newborn screening markers (C3, C3/C2, and C3/C16) present an inverse correlation with maternal vitamin B12 status in the first trimester of pregnancy. Regarding factors that may influence maternal serum vitamin B12 levels during the first trimester, smoking seems to have a negative effect, and meat consumption a positive effect.

Publication Type: Journal: Article

Source: EMBASE

Full Text:

Available from *Free Access Content* in [International Journal for Vitamin and Nutrition Research](#)

Title: Folate, Vitamin B12, Vitamin B6 and homocysteine: Impact on pregnancy outcome

Citation: Maternal and Child Nutrition, April 2013, vol./is. 9/2(155-166), 1740-8695;1740-8709 (April 2013)

Author(s): Furness D., Fenech M., Dekker G., Khong T.Y., Roberts C., Hague W.

Language: English

Abstract: Good clinical practice recommends folic acid supplementation 1 month prior to pregnancy and during the first trimester to prevent congenital malformations. However, high rates of fetal growth and development in later pregnancy may increase the demand for folate. Folate and vitamins B12 and B6 are required for DNA synthesis and cell growth, and are involved in homocysteine metabolism. The primary aim of this study was to determine if maternal folate,

vitamin B12, vitamin B6 and homocysteine concentrations at 18-20 weeks gestation are associated with subsequent adverse pregnancy outcomes, including pre-eclampsia and intrauterine growth restriction (IUGR). The secondary aim was to investigate maternal B vitamin concentrations with DNA damage markers in maternal lymphocytes. A prospective observational study was conducted at the Women's and Children's Hospital, Adelaide, South Australia. One hundred and thirty-seven subjects were identified prior to 20 weeks gestation as at high or low risk for subsequent adverse pregnancy outcome by senior obstetricians. Clinical status, dietary information, circulating micronutrients and genome damage biomarkers were assessed at 18-20 weeks gestation. Women who developed IUGR had reduced red blood cell (RBC) folate ($P < 0.001$) and increased plasma homocysteine concentrations ($P < 0.001$) compared with controls. Maternal DNA damage, represented by micronucleus frequency and nucleoplasmic bridges in lymphocytes, was positively correlated with homocysteine ($r = 0.179$, $P = 0.038$ and $r = 0.171$, $P = 0.047$, respectively). Multivariate regression analysis revealed RBC folate was a strong predictor of IUGR ($P = 0.006$). This study suggests that low maternal RBC folate and high homocysteine values in mid pregnancy are associated with subsequent reduced fetal growth. © 2011 Blackwell Publishing Ltd.

Publication Type: Journal: Article

Source: EMBASE

Full Text:

Available from *Wiley* in [Maternal and Child Nutrition](#)

Available from *Wiley* in [Maternal and Child Nutrition](#)

Title: Vitamin B12 deficiency and recurrent pregnancy loss: Is there an association?

Citation: Archives of Disease in Childhood: Fetal and Neonatal Edition, April 2013, vol./is. 98/(no pagination), 1359-2998 (April 2013)

Author(s): Bozreiba N.B., Cooley S.C., Coulter Smith S.C.S.

Language: English

Abstract: Introduction The importance of preconceptual folic acid has been established. However the metabolism of folate and Vitamin B12 is interlinked. Weak association has been described between Vitamin B12 deficiency and recurrent pregnancy loss. This has led to the implementation in some centres of routine B12 levels in patients with recurrent pregnancy loss. Our goal is to determine the value of such testing and its role in the management of these cases. Aim To determine whether the incidence of folate and/or Vitamin B12 deficiency is higher in patients with recurrent pregnancy loss than the reported national incidence of deficiency. Methods Retrospective review of all new referrals to the recurrent miscarriage clinic at the Rotunda Hospital Dublin. Vitamin B12 and folate levels were assessed at the initial consultation. Results National B12 levels and folate levels were accepted as 6% based on new nutritional data. We evaluated the folate and cobalamin status in 98 non-pregnant women with a history of recurrent spontaneous abortion (three or more consecutive) of unknown aetiology. Low Vitamin B12 was defined as serum value less than 190 ng/l, and serum folate values less than 4.5 ug/l were considered deficient. In total 7.1% ($n = 7$) patients were Vitamin B12 deficient and only one patient was folate deficient. This compares with a national incidence of 6%. These levels were not statistically different. Conclusion Serum concentrations of folic acid and Vitamin B12 are not significantly altered in women with unexplained recurrent miscarriage and we propose that routine testing is not warranted.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:

Available from *Highwire Press* in [Fetal and Neonatal](#)

Title: Maternal vitamin B12 levels during the first trimester of pregnancy and influence in newborn screening results

Citation: *Biochimica Clinica*, 2013, vol./is. 37/(S40), 0393-0564 (2013)

Author(s): Yahyaoui R., Dayaldasani A., Ruiz-Escalera J.F., Rodriguez-Espinosa M., Rueda I., Casero M.C., Perez- Valero V.

Language: English

Abstract: Background. During pregnancy, vitamin B12 concentrations may drop physiologically, and concentrations below reference values may not alter certain parameters. The reference range used for our general population is 254-1320 pg/mL. The use of non-pregnant values may not be appropriate for assessing vitamin B12 status during pregnancy. Methods. Serum vitamin B12 concentrations were evaluated in 204 pregnant women during the first trimester to calculate the reference interval (LOCI, Dimension Vista, Siemens Healthcare Diagnostics). To assess the effects of the variables BMI, vitamin supplements (including type and dosage), dietary intake, parity and smoking habits on vitamin B12 serum concentrations, stepwise multiple linear regression models using backward elimination were used. Other factors including the newborns' birthweight, and expanded newborn screening results (propionylcarnitine levels, C3/C2 and C3/C16 ratios) were considered. Results. The women participating in the study ranged in age from 15 to 46 (mean 30.0, SD6.11). The mean serum concentration of vitamin B12 was 502.4 pg/mL (SD 142.81). The reference range calculated was 272.7-837.8 pg/mL. Vitamin B12 concentrations were significantly lower in smokers, and in women with low meat consumption. The other factors did not have any significant effect. Newborns of mothers with lower vitamin B12 levels presented lower birthweight and higher propionylcarnitine levels, with higher C3/C2 and C3/C16 ratios. Conclusions. The reference interval for serum vitamin B12 concentrations obtained is narrower than the one currently used for our general population. Smoking seems to have a negative effect, and meat consumption a positive effect on vitamin B12 levels. Mothers with lower vitamin B12 concentrations during the first trimester of pregnancy seem to have children with lower birthweight and higher propionylcarnitine levels.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Title: Vitamin B(12) deficiency in infants secondary to maternal causes.

Citation: *CMAJ* : Canadian Medical Association journal = journal de l'Association medicale canadienne, Oct 2012, vol. 184, no. 14, p. 1593-1598, 1488-2329 (October 2, 2012)

Author(s): Roumeliotis, Nadia, Dix, David, Lipson, Alisa

Source: Medline

Full Text:

Available from *National Library of Medicine* in [CMAJ : Canadian Medical Association Journal](#)

Available from *ProQuest* in [Canadian Medical Association. Journal; CMAJ](#)

Available from *National Library of Medicine* in [CMAJ : Canadian Medical Association Journal](#)

Title: Evaluation of vitamin B12 levels during the first trimester of pregnancy

Citation: Journal of Inherited Metabolic Disease, September 2012, vol./is. 35/1 SUPPL. 1(S136), 0141-8955 (September 2012)

Author(s): Dayaldasani A., Yahyaoui R., Ruiz-Escalera J.F., Rodriguez-Espinosa M., Casero M.C., Rueda I., Perez-Valero V.

Language: English

Abstract: Background: During pregnancy, vitamin B12 concentrations may drop physiologically, and concentrations below reference values may not alter certain parameters. The use of non-pregnant values may not be appropriate for assessing vitamin B12 status during pregnancy. Method: Vitamin B12 concentrations were evaluated in 204 pregnant women during the first trimester to calculate the reference interval. Possible confounding factors were analyzed using stepwise multiple linear regression models. Other factors including the newborns' birthweight, and propionylcarnitine levels, as well as C3/C2 and C3/C16 ratios were considered. Results: The reference interval for vitamin B12 obtained was 272.7-837.8 pg/mL. Vitamin B12 concentrations were significantly lower in smokers, and in women with low meat consumption. Other factors did not have any significant effect. Newborns of mothers with lower vitamin B12 levels presented lower birth weight and higher propionylcarnitine levels, with higher C3/C2 and C3/C16 ratios. Conclusions: The reference interval for serum vitamin B12 concentrations obtained is narrower than the one currently used for our general population. Smoking seems to have a negative effect, and meat consumption a positive effect on vitamin B12 levels. Mothers with lower vitamin B12 concentrations during the first trimester of pregnancy seem to have children with lower birth weight and higher propionylcarnitine levels.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:

Available from *Springer Link Journals* in [Journal of Inherited Metabolic Disease](#)

Available from *ProQuest* in [Journal of Inherited Metabolic Disease](#)

Title: Low maternal vitamin B(12) is a risk factor for neural tube defects: a meta-analysis.

Citation: The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, Apr 2012, vol. 25, no. 4, p. 389-394, 1476-4954 (April 2012)

Author(s): Wang, Zhi-Ping, Shang, Xiao-Xiao, Zhao, Zhong-Tang

Abstract: The objective of this study was to assess whether low level of maternal vitamin B(12) is associated with an increased risk of fetal neural tube defects (NTDs), in order to contribute to research on further reduction of NTDs under a background of mandatory folic acid (FA) fortification. A meta-analysis was conducted. We retrieved and evaluated the studies published on the risk of low level of maternal vitamin B(12) for NTDs. The homogeneity of the studies was examined using the forest graph. Meta-analysis was applied to calculate the odds ratio (OR) of fetal NTDs in relation to low maternal B(12) and its 95% confidence interval (CI). We identified nine published articles including 567 cases and 1566 controls in the meta-analysis. All the studies selected were homogeneous according to the forest graph ($\chi^2 = 15.05$, $P < 0.1$). The estimated OR value of fetal NTDs in relation to low maternal B(12) was 2.41 (95% CI: 1.90-3.06). Low maternal B(12) status could be an important risk factor for the development of fetal NTDs. The addition of synthetic B(12) to current recommendations for periconceptual FA tablet supplements or FA-fortified foods should be considered.

Source: Medline

Full Text:

Available from *Taylor & Francis* in [Journal of Maternal-Fetal and Neonatal Medicine, The](#)

Title: Anaemia in pregnancy.

Citation: Best practice & research. Clinical obstetrics & gynaecology, Feb 2012, vol. 26, no. 1, p. 3-24, 1532-1932 (February 2012)

Author(s): Goonewardene, Malik, Shehata, Mishkat, Hamad, Asma

Abstract: Anaemia in pregnancy, defined as a haemoglobin concentration (Hb) < 110 g/L, affects more than 56 million women globally, two thirds of them being from Asia. Multiple factors lead to anaemia in pregnancy, nutritional iron deficiency anaemia (IDA) being the commonest. Underlying inflammatory conditions, physiological haemodilution and several factors affecting Hb and iron status in pregnancy lead to difficulties in establishing a definitive diagnosis. IDA is associated with increased maternal and perinatal morbidity and mortality, and long-term adverse effects in the new born. Strategies to prevent anaemia in pregnancy and its adverse effects include treatment of underlying conditions, iron and folate supplementation given weekly for all menstruating women including adolescents and daily for women during pregnancy and the post partum period, and delayed clamping of the umbilical cord at delivery. Oral iron is preferable to intravenous therapy for treatment of IDA. B12 and folate deficiencies in pregnancy are rare and may be due to inadequate dietary intake with the latter being more common. These vitamins play an important role in embryo genesis and hence any relative deficiencies may result in congenital abnormalities. Finding the underlying cause are crucial to the management of these deficiencies. Haemolytic anaemias rare also rare in pregnancy, but may have life-threatening complications if the diagnosis is not made in good time and acted upon appropriately. Copyright © 2011 Elsevier Ltd. All rights reserved.

Source: Medline

Title: B12 in fetal development.

Citation: Seminars in cell & developmental biology, Aug 2011, vol. 22, no. 6, p. 619-623, 1096-3634 (August 2011)

Author(s): Pepper, M Reese, Black, Maureen M

Abstract: Vitamin B12 (cobalamin) is necessary for development of the fetus and child. Pregnant women who are vegetarian or vegan, have Crohn's or celiac disease, or have undergone gastric bypass surgery are at increased risk of B12 deficiency. Low serum levels of B12 have been linked to negative impacts in cognitive, motor, and growth outcomes. Low cobalamin levels also may be related to depression in adults. Some studies indicate that B12 supplementation may improve outcomes in children, although more research is needed in this area. Overall, the mechanisms of B12 action in development remain unclear. Further studies in this area to elucidate the pathways of cobalamin influence on development, as well as to prevent B12 deficiency in pregnant women and children are indicated. Copyright © 2011 Elsevier Ltd. All rights reserved.

Source: Medline

Title: Pregnancy-specific reference ranges for haematological variables in a Scottish population

Citation: Journal of Obstetrics and Gynaecology, May 2011, vol./is. 31/4(286-289), 0144-3615;1364-6893 (May 2011)

Author(s): Shields R.C., Caric V., Hair M., Jones O., Wark L., McColl M.D., Ramsay J.E.

Language: English

Abstract: Using laboratory reference ranges, B<inf>12</inf> deficiency is inappropriately diagnosed and treated in pregnancy. We aim to define reference ranges for ferritin, folate, haemoglobin and B<inf>12</inf> in a pregnant population with advancing gestation. A total of 190 women participated in a cross-sectional study, 113 in the 1st and 77 in the 3rd trimester. All variables studied except red cell folate, decreased significantly from the 1st to the 3rd trimester. A total of 34% (64/190) of women were found to have 'xlow' B <inf>12</inf> as defined by traditional ranges. In women with anaemia and apparent B<inf>12</inf> deficiency, co-existing ferritin deficiency was demonstrated. All women with 'low' B<inf>12</inf> levels were invited to attend postnatally for re-testing. A total of 28% (18/64) attended, in whom all B <inf>12</inf> levels spontaneously increased. The use of gestation specific reference ranges for haematological variables may reduce inappropriate diagnosis of B<inf>12</inf> deficiency. In most women with apparent low B<inf>12</inf> levels and anaemia, ferritin deficiency was demonstrated. Therefore iron should be the initial management therapy. © 2011 Informa UK, Ltd.

Publication Type: Journal: Article

Source: EMBASE

Full Text:

Available from *Taylor & Francis* in [Journal of Obstetrics and Gynaecology](#)

Title: Neurological manifestations of severe vitamin B12 deficiency in infants

Citation: *Developmental Medicine and Child Neurology*, January 2011, vol./is. 53/(37-38), 0012-1622 (January 2011)

Author(s): Balu R., Sharrard M.J., Mordekar S.R.

Language: English

Abstract: Objective: To describe four infants with neurological manifestations of severe vitamin B12 deficiency secondary to maternal vitamin B12 deficiency. Method: Retrospective case notes review. Results: Four infants (three females, one male) presented between 3 and 10 months of age. They were all born by normal delivery after an uneventful pregnancy. They were exclusively breast fed for initial 5 to 6 months. All infants had failure to thrive, vomiting or gastro-esophageal reflux and weaning difficulties. Neurological manifestations included developmental delay (two infants); developmental regression (one); seizures (one), which included atypical absences and clusters of generalized tonic-clonic seizures; encephalopathic presentation (two); and acquired microcephaly (two). Diagnosis was confirmed by elevated urinary methyl malonate and plasma homocysteine; and low vitamin B12 levels in infants and mothers. Macrocytic anaemia was seen in two infants. Other neurometabolic investigations were normal. Pernicious anaemia was subsequently diagnosed in two mothers. Treatment with parenteral vitamin B12 in all infants showed good biochemical and developmental response. There was improvement in feeding pattern, weight and head circumference. Neurodevelopmental outcome has been good with a follow up period varying from 6 to 18 months. The infant who presented with seizures, developed epileptic spasms at 9 months age and responded well to treatment with steroids. Conclusion: Vitamin B12 deficiency in infants is preventable. It should be considered as a differential diagnoses in breastfed infants with failure to thrive, reflux and developmental arrest. Maternal B12 deficiency in pregnancy is often not detected because of simultaneous iron deficiency masking the macrocytosis. Urinary methylmalonate could be a useful, sensitive screening test in the third trimester of pregnancy. It provides a functional assessment of B12 sufficiency in an individual who may be asymptomatic and not anaemic.

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text:

Available from *Wiley-Blackwell Free Backfiles NHS* in [Developmental Medicine and Child Neurology](#)

Available from *Wiley* in [Developmental Medicine and Child Neurology](#)

Available from *ProQuest* in [Developmental Medicine and Child Neurology](#)

Available from *Wiley* in [Developmental Medicine and Child Neurology](#)

Available from *Wiley* in [Developmental Medicine and Child Neurology](#)

Title: Newborn vitamin B12 deficiency

Citation: Journal of Pediatrics, July 2010, vol./is. 157/1(A3), 0022-3476 (July 2010)

Author(s): Welch T.R.

Language: English

Publication Type: Journal: Article

Source: EMBASE

Full Text:

Available from *Journal of Pediatrics* in [Patricia Bowen Library and Knowledge Service West Middlesex university Hospital](#)

Title: Clinical manifestations of infants with nutritional vitamin B<inf>12</inf> deficiency due to maternal dietary deficiency

Citation: Acta Paediatrica, International Journal of Paediatrics, January 2009, vol./is. 98/1(98-102), 0803-5253;1651-2227 (January 2009)

Author(s): Zengin E., Sarper N., Caki Kilic S.

Language: English

Abstract: Aim: In developing countries, nutritional vitamin B<inf>12</inf> deficiency in infants due to maternal diet without adequate protein of animal origin has some characteristic clinical features. In this study, haematological, neurological and gastrointestinal characteristics of nutritional vitamin B <inf>12</inf> deficiency are presented. Methods: Hospital records of 27 infants diagnosed in a paediatric haematology unit between 2000 and 2008 were evaluated retrospectively. Results: The median age at diagnosis was 10.5 months (3-24 months). All the infants were exclusively breast fed and they presented with severe nonspecific manifestations, such as weakness, failure to thrive, refusal to wean, vomiting, developmental delay, irritability and tremor in addition to megaloblastic anaemia. The diagnosis was confirmed by complete blood counts, blood and marrow smears and serum vitamin B<inf>12</inf> and folic acid levels. The median haemoglobin level was 6.4 g/dL (3.1-10.6) and mean corpuscular volume (MCV) was 96.8 fL (73-112.3). Some patients also had thrombocytopenia and neutropenia. All the infants showed clinical and haematological improvement with vitamin B<inf>12</inf> administration. Patients with severe anaemia causing heart failure received packed red blood cell transfusions as the initial therapy. Conclusion: Paediatricians must consider nutritional vitamin B <inf>12</inf> deficiency due to maternal dietary deficiency in the differential diagnosis of some gastrointestinal, haematological, developmental and neurological disorders of infants with poor socioeconomic status. Delay in diagnosis may cause irreversible neurological damage. © 2008 The Author(s).

Publication Type: Journal: Article

Source: EMBASE

Full Text:

Available from Wiley in [Acta Paediatrica](#)

Available from Wiley in [Acta Paediatrica](#)

Title: Effects of folate and vitamin B12 deficiencies during pregnancy on fetal, infant, and child development.

Citation: Food and nutrition bulletin, Jun 2008, vol. 29, no. 2 Suppl, p. S101, 0379-5721 (June 2008)

Author(s): Molloy, Anne M, Kirke, Peadar N, Brody, Lawrence C, Scott, John M, Mills, James L

Abstract: The importance of folate in reproduction can be appreciated by considering that the existence of the vitamin was first suspected from efforts to explain a potentially fatal megaloblastic anemia in young pregnant women in India. Today, low maternal folate status during pregnancy and lactation remains a significant cause of maternal morbidity in some communities. The folate status of the neonate tends to be protected at the expense of maternal stores; nevertheless, there is mounting evidence that inadequate maternal folate status during pregnancy may lead to low infant birthweight, thereby conferring risk of developmental and long-term adverse health outcomes. Moreover, folate-related anemia during childhood and adolescence might predispose children to further infections and disease. The role of folic acid in prevention of neural tube defects (NTD) is now established, and several studies suggest that this protection may extend to some other birth defects. In terms of maternal health, clinical vitamin B12 deficiency may be a cause of infertility or recurrent spontaneous abortion. Starting pregnancy with an inadequate vitamin B12 status may increase risk of birth defects such as NTD, and may contribute to preterm delivery, although this needs further evaluation. Furthermore, inadequate vitamin B12 status in the mother may lead to frank deficiency in the infant if sufficient fetal stores of vitamin B12 are not laid down during pregnancy or are not available in breastmilk. However, the implications of starting pregnancy and lactation with low vitamin B12 status have not been sufficiently researched.

Source: Medline

Full Text:

Available from *Free Access Content* in [Food and Nutrition Bulletin](#)

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