



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



Mary F.F. Chong^{a,b,e,*}, Jocelyn X.Y. Wong^b, Marjorelee Colega^b, Ling-Wei Chen^c, Rob M. van Dam^c, Chuen Seng Tan^c, Ai Lin Lim^b, Shirong Cai^f, Birit F.P. Broekman^{b,d}, Yung Seng Lee^{a,b,e}, Seang Mei Saw^c, Kenneth Kwek^{g,k}, Keith M. Godfrey^{h,i}, Yap Seng Chong^{b,f}, Peter Gluckman^{a,b,j}, Michael J. Meaney^{b,k}, Helen Chen^{g,l}, on behalf of GUSTO study group

^a Clinical Nutrition Research Centre, Singapore Institute for Clinical Sciences, A*STAR, Singapore

^b Singapore Institute for Clinical Sciences, A*STAR, Singapore

^c Saw Swee Hock School of Public Health, Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore

^d Psychological Medicine, Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore

^e Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore

^f Obstetrics & Gynaecology, Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore

^g KK Women's and Children's Hospital, Singapore

^h MRC Lifecourse Epidemiology Unit and NIHR Southampton Biomedical Research Centre, University of Southampton

ⁱ University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom

^j Liggins Institute, Auckland, New Zealand

^k McGill University, Montreal, Canada

^l Duke-National University of Singapore, Singapore

ARTICLE INFO

Article history:

Received 6 February 2014

Received in revised form

2 April 2014

Accepted 4 April 2014

Keywords:

Folate

Vitamin B12

Pregnancy diet

Antenatal depression

Postnatal depression

Edinburgh Postnatal Depression Scale

ABSTRACT

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 \pm 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.

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* Corresponding author. Clinical Nutrition Research Centre, 14 Medical Drive, #07-02, MD6 Building, Singapore 117599, Singapore. Tel.: +65 6407 4364; fax: +65 6774 7134.

E-mail address: mary_chong@sics.a-star.edu.sg (M.F.F. Chong).

1. Introduction

The link between nutrition and mood is well-documented and a number of nutrients have been linked with depression in the

general population (Astorg et al., 2008; Dimopoulos et al., 2007; Gilbody et al., 2007; Kaplan et al., 2007). While pregnant mothers are more susceptible to nutrient deficiencies because of the demands of the growing fetus (Bodnar and Wisner, 2005), and continue to be so several months after childbirth due to delayed postpartum repletion and lactation (Leung and Kaplan, 2009), only recently has research on the role of nutrients in relation to depression during the antenatal (Freeman, 2006; Jans et al., 2010; Leung and Kaplan, 2009) and postpartum periods (Soh et al., 2009; Strom et al., 2009) begun to emerge.

Perinatal or peripartum depression refers to major and minor depressive episodes during pregnancy (antenatal) or within the first 12 months after delivery (postnatal) (Gavin et al., 2005). Perinatal depression can have serious and long-lasting consequences for both the mother and child. Depressed mothers are known to lose focus easily, express more negative emotions, experience social withdrawal and have poorer appetite (Klainin and Arthur, 2009; Lee and Chung, 2007). Consequently, depression is often associated with poor maternal self-care and health outcomes (Bennett et al., 2004; Canadian Paediatric Society Position Statement, 2004; Stein et al., 2008), which can influence the mother–child interaction (McManus and Poehlmann, 2012) and in turn negatively impact the growth and cognition development of the fetus and child (Gibson et al., 2009).

Low levels of the B vitamins have been linked to depression, with different B vitamins implicated in particular study populations. While vitamin B12 (cobalamin) showed a strong correlation with depression in elderly population (Robinson et al., 2011; Tiemeier et al., 2002), correlations between folate and depression have been reported in adult and adolescent populations (Beydoun et al., 2010; Murakami et al., 2010). Proposed mechanisms for these associations include the neuronal hypothesis, which suggests decreased synthesis of neurotransmitters serotonin, dopamine and noradrenaline as a consequence of the low levels of these B vitamins, and the ‘vascular’ hypothesis, which implicates hyperhomocysteinaemia associated vascular damage and chronic inflammation, stemming from deficiency in the B vitamins (Ellsworth-Bowers and Corwin, 2012).

To date, only a few studies have examined the relationships between B vitamins and perinatal depression. Lewis et al. found no association between folic supplementation during pregnancy (18 and 32 weeks) and the risk of depression during pregnancy and up to 8 months after pregnancy (Lewis et al., 2012). In two other cohort studies, dietary folate, vitamin B12 and B6 intakes (Miyake et al., 2006) and red blood cell folate concentrations (Blunden et al., 2012) showed no associations with postnatal depression (Blunden et al., 2012; Lewis et al., 2012; Miyake et al., 2006). We investigate the associations of maternal folate and vitamin B12 concentrations during pregnancy with probable antenatal and early postnatal depression in a prospective cohort of Asian mothers from three ethnic groups.

2. Subjects and methods

This study was part of the GUSTO study, which is the first prospective mother–offspring cohort study in Singapore involving detailed assessments of pregnant women and characterisation of their offspring from birth onwards (Soh et al., 2012). The study was granted ethical approval by the Institutional Review Boards of respective hospitals. Written informed consent was collected from all participants upon recruitment.

3. Study design

Pregnant women attending antenatal care (<14 weeks’ gestation) in KK Women’s and Children’s Hospital (KKH) and National

University Hospital (NUH), which house the major public maternity units in Singapore handling one third of the country’s births annually, were recruited into the GUSTO study from June 2009 to September 2010. More detailed information about this cohort study has been recently published (Soh et al., 2013). In brief, the inclusion criteria included age range between 18 and 50 years, intention to finally deliver in KKH or NUH, intention to reside in Singapore for the next 5 years, and willingness to donate cord, cord blood, and placenta. Only Chinese, Malay, and Indian women whose parents and whose husband’s parents were of the same ethnicity were included in the study. Women with the following pre-existing health conditions were excluded: type 1 diabetes mellitus, current depression or mental health-related disorders.

Women recruited in their first trimester returned to the hospital at 26th–28th week of gestation for a follow-up visit. Detailed interviews were conducted during this clinic visit to obtain demographic data, such as socioeconomic status, educational attainment, smoking status, alcohol status, medications, personal health and family medical history. A mother was defined to be a regular smoker if she smoked once a day for a year or longer. Smoke exposure was defined as having at least one person at home smoking on a daily basis for 6 months and longer. Fasting blood samples were also drawn between 26th and 28th week of gestation, centrifuged and plasma stored at -80°C for assay. The women were also asked to complete the Edinburgh Postnatal Depression Scale (EPDS), a self-administered questionnaire, during this visit and subsequently after delivery, during a 3-month postnatal home visit.

4. Maternal folate and vitamin B12 concentrations

Of the 1162 women enrolled, 1000 mothers with singleton live births had available blood samples for measurement of plasma folate and vitamin B12. The analyses of folate and vitamin B12 concentrations were conducted at the NUHS Referral laboratory using the competitive electrochemiluminescence immunoassay on the ADVIA Centaur Immunoassay System. Between-run CVs for plasma measurements were as follows: 6.0%–10.5% between 4.1 nmol/L and 22.3 nmol/L with an analytic range of 1.45–45.4 nmol/L for plasma folate; 4.3%–8.8% between 160 pmol/L and 490 pmol/L with an analytic range of 22–1476 pmol/L for plasma vitamin B12.

5. Assessment of depressive symptoms and low mood

The EPDS is a 10-item self-reported screening questionnaire that had been devised to screen for probable depression. Each question has a score of 0–3 and the total score ranges from 0 to 30. An EPDS score of ≥ 15 and ≥ 13 was used to identify probable cases of “antenatal depression” and “postnatal depression” (Matthey et al., 2006), respectively, based on validity studies which demonstrated specificity 98% and sensitivity of 57%, for antenatal depression (Gibson et al., 2009; Stein et al., 2008), and specificity of 95–96.7% and a sensitivity of 41–86.7% for postnatal depression (Chen et al., 2013; Lee et al., 1998). There is a possibility that some cases of depression would still have been missed due to the relatively low sensitivity of the EPDS.

6. Subjects

Among the 999 GUSTO participants who had their plasma folate and vitamin B12 concentrations successfully measured, 967 participants completed the EPDS questionnaire at 26th weeks, while 719 participants completed the EPDS questionnaire at 3 months postpartum. Of the 32 who did not provide EPDS data at 26th week,

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