Reviewer's report

**Title:** Subclinical iron deficiency is a strong predictor of bacterial vaginosis in early pregnancy

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**Reviewer:** Phillip Hay

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**General**

Subclinical iron deficiency is a strong predictor of bacterial vaginosis in early pregnancy

Bacterial vaginosis is an important risk factor for adverse pregnancy outcomes and acquisition of sexually transmitted infections including HIV. Those women who experience frequent recurrences of bacterial vaginosis after treatment also experience distress and frustration from their condition. It is likely that most women develop bacterial vaginosis at some stage although it may well remain asymptomatic. Our lack of understanding of the factors which predispose to relax of bacterial vaginosis is reflected in our inability to control it.

This paper reports a study investigating iron status in early pregnancy in relation to the diagnosis of intermediate flora and bacterial vaginosis. Natural history study suggests that BV becomes less common during a pregnancy and may well go through the intermediate stage before becoming normal(1). It therefore appears appropriate to classify intermediate and bacterial vaginosis as abnormal flora for the purposes of a study like this. This is a substudy of a larger study investigating risk factors for preterm birth. The authors refer to recent findings identifying associations between genetic differences such as mutations in the Toll 4-like receptor gene and phenotypic differences in the expression of anti inflammatory cytokines as being associated with susceptibility to bacterial vaginosis. Their hypothesis was that micronutrient status might also affect the incidence of BV. Iron in particular is known to affect bacterial colonisation. The principal finding was that conventional markers of iron deficiency such as haemoglobin and serum ferritin were not associated with abnormal vaginal flora, but more sensitive and specific indicators of iron deficiency including soluble transfer and receptor levels and the log [sTfR/ferritin] index were significantly associated with abnormal flora. They concluded that subclinical iron deficiency probable related to inadequate preconceptional iron status was a risk factor for abnormal vaginal flora in early pregnancy.

The women were screened at a median of 9.2 weeks of gestation. In the discussion the authors identify many of the limitations of the study which include the small sample size with only 18 women with abnormal flora and 80 with normal flora. Clearly these findings need to be confirmed in larger prospective cohort studies. They controlled for most of the established confounders including age, gestational age, body mass index, smoking habit and parity, but did not collect data on sexual behaviour related characteristics and did not present data on ethnicity which may be an important risk factor for bacterial vaginosis and could also be related to iron status. They identified a cut-off sTfR levels but the sensitivity and positive predictive value were actually quite low for disturbed vaginal flora.

Many of the women had been taking iron supplementation during the pregnancy but this may not yet have had time to alter the iron stores. Again the study did not have the power to examine this in a meaningful way. The authors conclude that if iron status is important, it would be better to correct it
in a preconceptional phase than during an established pregnancy.

This is an interesting study and gives us one more risk factor to consider in the etiology of bacterial vaginosis. It does need to be replicated and it would be interesting to examine a non pregnant population.

Natural history study suggests that BV becomes less common during a pregnancy and may well go through the intermediate stage before becoming normal. It therefore appears appropriate to classify intermediate and bacterial vaginosis as abnormal flora for the purposes of a study like this.

I do not feel qualified to comment on the statistics used, although they appear valid.

Reference List