Title: Iron Deficiency Screening in Non-anemic, First Trimester Gravidas

NCT# 03670537

April 11, 2018

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The 2015 United States Preventive Services Task Force (USPSTF) stated “there is insufficient evidence to recommend the routine screening for iron deficiency in non-anemic gravidas” (Cantor, AIM 2015). The basis for this recommendation is the lack maternal or fetal outcome data in this population. To date, there are no guidelines for the treatment of non-anemic, iron deficiency pregnancy women with or without anemia. iObstetricians and gynecolgists often do not screen for iron deficiency unless the mean corpuscular volume (MCV) is reduced even in the presence of a reduced hemoglobin. Iron deficiency occurs prior to a decrement in hemoglobin concentration, followed by a decrease in the MCV which occurs after. Subsequently, if these recommendation are followed up to 50% of iron deficient pregnant women remain undiagnosed.

While prospective studies may be absent proving that routine screening and supplementation is beneficial, there is ample evidence that iron deficiency in mothers and infants results in significant morbidity, even in the absence of anemia. Fetal, neonatal and childhood brain growth and development require iron, with deficiencies resulting with adverse effects on myelination, neurotransmitter synthesis and brain programming (Roncaglio, Am J of Clin Nutr, 1998). There is a two-fold incidence of preterm birth, three-fold increase in low birth weight and small for gestational age infants. In addition to negative effects on the fetus, maternal iron deficiency is associated with an increased risk for caesarean delivery, transfusion, perinatal bleeding, pre-eclapsia, placental abruption, poor wound healing, cardiac failure and even death (Drukker Transfusion 2015, Zimmerman J Clin Endocrin Metab 2007, Auerbach Am J Med 2017). Of note, using existing guidelines infants are not screened for iron deficiency even if they are at high risk (preterm, infants of diabetic mothers (Cheng J Peds 2012), smokers or those with intrauterine growth restriction (Siddappa Neonatology 2007).

Published evidence suggests that when iron deficiency is present later in pregnancy in the mother, adequate iron delivery to the fetus does not occur. In a prospective study of 2400 urban women with iron deficiency in the second and third trimesters, while supplementation resulted in a significant improvement in maternal hemoglobin concentrations and iron parameters, over 45% of infants were iron deficient at birth.

Subsequently, while prospective studies are lacking supporting routine screening and iron supplementation, high quality published evidence imputing a litany of morbid events associated with iron deficiency, calls into question the recommendations of the USPSTF. Until such evidence is available based on the preponderance of evidence supporting absence of harm with either screening or supplemention we believe all gravidas presenting to their obstetricians should be screened for iron deficiency.

We propose a prospective observation study of one hundred consecutive, non-selected, non-anemic, first trimester pregnant women to have iron parameters added to their routine laboratory tests. While we realize this is not standard, many practices already have adopted this screening process. We intend to redact all demographic patient information and expect to incur no uncovered costs. As a result we believe neither investigational review board or informed consent is necessary. In hundreds of patients so screened we have encountered no insurance pushback. The additional tests will include only serum iron, total iron binding capacity (TIBC), percent transferrin saturation (Fe/TIBC) and serum ferritin. The data will be stratified by parity.

We anticipate to find an incidence of iron deficiency of 30-40% based on either a low TSAT or low serum ferritin. Such a finding should motivate properly powered, prospective outcome analyses supporting a new paradigm that incorporating the low cost screening for iron deficiency accompany standard screening tests at the beginning of pregnancy irrespective of the presence or absence of anemia.

There was no pre-specified plan for statistical analysis.