Elevated Ferritin Levels During First Trimester Associated With GDM

Written by Toni Rizzo

Gestational diabetes mellitus (GDM) can lead to short- and long-term health risks for both the mother and the infant, including increased risk of type 2 diabetes later in life. Recent evidence shows that excess iron stores are associated with an increased risk of diabetes. Moderately elevated ferritin levels, though well below those observed in iron overload disorders, have been associated with increased insulin secretion, decreased insulin sensitivity, and type 2 diabetes. However, the level of elevation at which this increased risk begins has not been established.

The proposed mechanisms for the association of an elevated ferritin level with increased diabetes risk include excess iron and inflammation. A randomized controlled trial in nonanemic pregnant women revealed that daily iron supplementation increased ferritin levels but did not increase the risk of GDM [Chan KKL et al. *BJOG* 2009]. Case-control studies that looked at the association of GDM in pregnant women and high ferritin levels have not indicated a clear association after controlling for inflammation [Sharifi F et al. *Diabetes Metab Syndr Obes* 2010; Chen X et al. *Diabetes Care* 2006]. Amina Khambalia, PhD, University of Sydney, Sydney, Australia, presented results of a retrospective study that aimed to determine whether an elevated serum ferritin level during the first trimester is associated with subsequent GDM when there is no evidence of inflammation.

Patients in the first trimester of pregnancy (n = 3143) had clinical and laboratory data collected. Women with preexisting diabetes, multiple pregnancies, or C-reactive protein (CRP) > 5 mg/L were excluded. Stored blood samples were tested for serum ferritin, soluble transferrin receptor (sTfR), and CRP. Birth data and hospital data records on GDM were linked for the remaining 3045 pregnancies. Among these, 3.6% (n = 110) developed GDM.

The development of GDM was associated with maternal age ≥ 35 years ($p < .004$), gestational age > 12 weeks ($p = .06$), weight ≥ 75th percentile ($p = .05$), and geography ($p = .002$). On univariate analysis, median ferritin levels were significantly higher among women with GDM (33.9 µg/L) compared with women without GDM (25.9 µg/L; $p = .0007$; Table 1). There was no significant difference in sTfR levels between the 2 groups. Fewer women with GDM were iron deficient (7.4%) compared with women without GDM (18.8%; $p = .005$). Women with GDM were more likely to have ferritin levels in the highest tertile (46.3% vs 32.6%; $p = .005$) and 75th percentile (33.7% vs 24.7%; $p = .05$) when compared to women without GDM.

Multivariate analysis adjusting for maternal age, parity, country of birth, weight, gestational age at blood collection, smoking, and CRP, revealed that ferritin was still associated with a statistically significant increased risk of developing GDM (adjusted odds ratio, 1.44; 95% CI, 1.10 to 1.90).

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Table 1. Univariate Analysis of Iron Status in Women With and Without GDM

Iron Levels	GDM, Median (Q1, Q3)	No GDM, Median (Q1, Q3)	p Value
Ferritin, µg/L	33.9 (19.6, 63.8)	25.9 (14.6, 43.5)	.0007
sTfR, nmol/L	15.7 (12.6, 18.7)	14.8 (11.9, 18.2)	.13
Ferritin Categories	**GDM, %**	**No GDM, %**	
Iron deficient, < 12.0 µg/L	7.4	18.8	.005
Highest tertile, ≥ 36.4 µg/L	46.3	32.6	.005
75th percentile, ≥ 43.9 µg/L	33.7	24.7	.05

GDM=gestational diabetes mellitus; sTfR=soluble transferrin receptor.

These results showed evidence of an association between elevated ferritin level and risk of developing GDM among women without evidence of inflammation. Transferrin receptor levels were not associated with the development of GDM. Future studies are needed to confirm these results, to determine if there is utility in the routine measurement of ferritin, and to identify other markers of iron and inflammation.

Antihypertensive and Vascular Benefits of Blueberries in Postmenopausal Women

Written by Brian Hoyle

Daily consumption of about 1 cup of fresh blueberries may help reduce arterial stiffness and decrease blood pressure (BP) by improving vasodilation due to the increased production or bioavailability of nitric oxide (NO), said Sarah A. Johnson, PhD, RD, CSO, Florida State University, Tallahassee, Florida, USA.

Hypertension (HTN) is a modifiable risk factor for cardiovascular disease (CVD) [Go AS et al. *Circulation* 2013; Rosamond W et al. *Circulation* 2008]. HTN currently affects >77 million Americans [Go AS et al. *Circulation* 2013]. Postmenopausal women seem to be affected disproportionately. [Barton M, Meyer MR. *Hypertension* 2009; Rosenthal T, Oparil S. *J Hum Hypertens* 2000]. The causes of HTN are multifactorial but are partly due to endothelial dysfunction, which results in decreased vasodilation and increased vasoconstriction. Endothelial dysfunction also increases stiffness of arteries, which is involved in the development and progression of both HTN and CVD [Wallace SML et al. *Hypertension* 2007; Bonetti PO et al. *Arterioscler Thromb Vasc Biol* 2003; Taddei S et al. *Curr Pharm Dis* 2003; Widlansky ME et al. *J Am Coll Cardiol* 2003; Koh KK et al. *J Am Coll Cardiol* 2001].

The treatment of BP in prehypertensive individuals and those with stage 1 HTN focuses on lifestyle modifications (eg, diet) [Chobanian AV. *Hypertension* 2003]. The polyphenol constituents of berries, including blueberries, appear to be beneficial in reducing cardiovascular risk, as judged from their effects on BP, endothelial function, and arterial stiffness [Rodriguez-Mateos A et al. *J Agric Food Chem* 2013; Basu A et al. *Nutr Rev* 2010]. However, the influence of blueberries on arterial stiffness measured by pulsed wave velocity (PWV) had not previously been studied.

Dr. Johnson and colleagues hypothesized that eating 22 g of freeze-dried blueberry powder daily for 8 weeks would reduce arterial stiffening and improve endothelial function, in turn reducing BP. The double-blind placebo-controlled trial comprised 48 postmenopausal women with pre-HTN or stage 1 HTN. They were randomly assigned to receive the daily blueberry powder (n=20) or the same daily quantity of placebo powder (n=20). Brachial BP and brachial-ankle and carotid-femoral pulsed wave velocity were measured at baseline, 4 weeks, and 8 weeks. Plasma levels of NO were measured at the same times.

Table 1. Effects of Blueberries on Blood Pressure

	Systolic Blood Pressure (mm Hg)		Diastolic Blood Pressure (mm Hg)	
	Blueberry	Control	Blueberry	Control
Baseline	138	138	80	78
4 week	136	136	77	78
8 week	131[a]	139	75[b]	80

[a]Significant difference ($p < .05$) compared with baseline. [b]Significant difference ($p < .01$) compared with baseline.

Table 2. Effects of Blueberries on Arterial Stiffness

	Brachial-Ankle Pulse Wave Velocity (cm/s)	
	Blueberry	Control
Baseline	1498	1470
4 week	1464	1466
8 week	1401[a]	1477

[a]Significant difference ($p < .05$) compared with baseline.