SHBG INTEGRATES THE CARDIOVASCULAR RISK AND METABOLIC DYSFUNCTION OF GESTATIONAL OBESITY

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Background:

Sex hormone-binding globulin (SHBG) is the major sex steroid carrier protein. Its production is negatively regulated by insulin and monosaccharides. The concentration of SHBG increases between 16 and 27 weeks gestation and is negatively associated with pre-gestational body mass index (BMI) and weight gain during pregnancy. The link of SHBG with cardiovascular risk is poorly understood.

Objetive:

In obese pregnant women, we aimed to study the association of circulating SHBG with cardiovascular risk factors independently of endocrine-metabolic parameters.

Methods:

Fasting serum SHBG levels were quantified between 24 and 28 weeks of gestation in 160 healthy pregnant women (87 with normal weight and 73 with pre-pregnancy obesity and/or gestational obesity, as defined by international references). Cardiovascular risk parameters [C-reactive protein (CRP) and blood pressure (BP)], metabolic parameters [glycosylated haemoglobin (HbAc1), pre and post-load glucose, C-peptide, insulin (and insulin resistance index [HOMA-IR]), triglycerides and high molecular weight adiponectin (HMW)], and endocrine parameters [total testosterone and estradiol] were also assessed.

Results:

As expected, lower concentrations of SHBG were associated with increased body mass index (BMI), HbA1c, pre and post-load glucose, C-peptide, HOMA-IR, triglycerides and less HMW adiponectin; lower SHBG was also associated with more CRP and BP ($p<0.01$ to $p<0.0001$ for all comparisons). These associations were more robust in women with obesity, who had lower SHBG concentrations compared to normal-weight women (510±15 vs 595±14 nmol/L; $p<0.0001$). In multivariate analysis in obese women, SHBG showed independent associations with CRP ($\beta=-0.377$, $p<0.001$; $R2=16.7$) and BP ($\beta=-0.255$, $p=0.030$; $R2=6.4$) independently of maternal age, BMI, metabolic (HOMA-IR and HbAc1) and endocrine (testosterone and estradiol) parameters.

Table 1. Correlation coefficients for SHBG with metabolic and cardiovascular risk parameters.

SHBG	All (n=160)		Normal weight (n=87)		Obese (n=73)	
	r	p	r	p	r	p
BMI (kg/m²)	-0.442	<0.0001	-0.237	0.030	-0.367	0.002
Fasting glucose(mg/dL)	-0.187	<0.01	-0.120	ns	-0.277	<0.01
Post-load glucose (mg/dL)	-0.203	<0.01	-0.064	ns	-0.337	<0.01
C-peptide (ng/mL)	-0.328	<0.0001	-0.086	ns	-0.391	<0.001
HOMA-IR	-0.220	<0.01	0.042	ns	-0.306	<0.01
Triglycerides (mg/dL)	-0.197	<0.01	-0.134	ns	-0.227	<0.05
HbA1c (%)	-0.178	<0.01	-0.036	ns	-0.390	<0.001
HMW adiponectin (mg/L)	0.297	<0.0001	0.236	<0.05	0.238	<0.05
BP (mmHg)	-0.216	<0.01	-0.115	ns	-0.327	<0.01
CRP (mg/L)	-0.364	<0.0001	-0.268	0.031	-0.418	<0.001

Table 2. Multivariate analysis between SHBG and cardiovascular risk parameters.

SHBG	All			Normal weight			Obese		
	Beta	Sig.	R²	Beta	Sig.	R²	Beta	Sig.	R²
CRP (mg/L)	-0.256	0.003	5.6%	-0.262	0.033	6.7%	-0.377	<0.0001	16.7%
BP (mmHg)	--	--	--	--	--	--	-0.255	0.032	6.4%
BMI (kg/m²)	-0.347	<0.0001	20,1%	-0.306	0.013	12.4%	--	--	--

Conclusion:

SHBG is decreased in obese pregnant women in association with a less favorable cardiovascular profile. We suggest that SHBG can integrate the cardiovascular risk and metabolic dysfunction of gestational obesity.