

## Maternal Obesity: Population Trends, Inflammatory Profiles and Immune Dysregulation

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**Background:** Large population-based studies suggest increased risks of antenatal, intrapartum, and neonatal complications secondary to obesity in pregnancy. Obesity during pregnancy is associated with a pro-inflammatory state as well as immune dysregulation; factors known to influence neonatal outcome. The potential associations between serum levels of cytokines and the weight status of the gravida are largely unknown.

**Objective:** 1) To examine time trends of obesity prevalence in pregnant women, and 2) to evaluate the hypothesis that obesity in pregnancy is associated with increased levels of pro-inflammatory and immunomodulatory cytokines/growth factors.

**Methods:** Population-based information was obtained from the Maine State Birth Records Database and evaluated for prevalence and degree of obesity (defined as early second trimester BMI  $\geq 30$ ) from 1981-2005. A pilot study was performed using maternal serum collected in the early second trimester examining several biomarkers associated with the inflammatory process by ELISA. Values were compared relative to maternal body mass index (BMI) among four weight categories: normal (BMI 20-26.5), overweight (BMI 26.6-31), obese (BMI 31.1-41), and morbidly obese (BMI  $>41$ ) (n=80; 20 from each weight group). Statistical analyses were performed by Kruskal-Wallis ANOVA.

**Results:** Among 219,173 pregnant women, mean second trimester weight increased linearly from 139 pounds in 1981 to 161 pounds in 2005, at a rate of approximately one pound per year (**Table 1**). To account for maternal age-related trends with median primiparous ages increasing over the studied time period, 27 year old mothers were examined for the 25 year period and the median weight gain was also 25 pounds in 25 years. Macrophage Chemotactic Protein (MCP)-1, Leptin, and C-reactive protein (CRP) were statistically significantly different between the groups. Comparisons of groups revealed that MCP-1 (p=0.002); Leptin (p<0.001) and CRP were significantly increased with morbid obesity (p<0.001) (**Table 2**). Interleukin (IL)-2 tended to exhibit a U-shaped relationship with body weight and the distribution of transforming growth factor (TGF)- $\beta$ -1 levels tended to widen with decreasing body mass.

**Conclusions:** Median maternal weight has increased significantly over time. Maternal obesity is associated with upregulation of several pro-inflammatory factors which might be transmitted to the fetus and influence neonatal outcome. These findings provide the basis for future research regarding the complex interactions between maternal obesity and complications of pregnancy in the mother and infant.

Table 1: Trends in Maternal Weights in 25 years

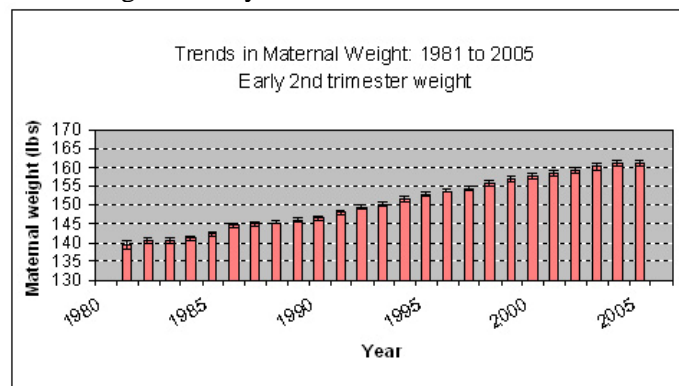


Table 2: Markers of Inflammation by BMI category

Markers	Normal BMI n=20	Over Wt. BMI n=19	Obese BMI n=21	Morbidly Obese BMI n=20	p-value
MCP	323 (265 - 381)	329 (242-346)	315 (208-361)	387 (359-430)	0.002
TNF	3.8 (1.6-8.3)	3.6 (1.9-5.7)	4.5 (2.7-6.9)	4.47 (1.36-11.3)	0.77
TGF	12.4 (8.9-15.9)	11.1 (9.2-13.3)	10.5 (8.9-12.1)	10.6 (8.40-11.3)	0.45
Leptin	12.4 (8.4-16.7)	25.5 (21.4-33.1)	30.4 (24.2-35.7)	49.6 (38.6-54.9)	<0.001
HGF	1.40 (1.2-1.8)	1.44 (1.1-1.7)	1.62 (1.3-2.1)	1.47 (1.07-1.59)	0.38
IL-2	1.45 (0.0-3.8)	0.95 (0.0-4.0)	0.00 (0.0-2.0)	1.70 (0.00-3.98)	0.46
hsCRP	0.28 (0.17-0.39)	0.71 (0.31-0.92)	0.75 (0.54-1.3)	1.44 (0.94-1.71)	<0.001

All values are medians (interquartile ranges). Statistical analysis performed using Kruskal-Wallis ANOVA test.