

Maternal Obesity and Risk of Fetal Congenital Abnormality

Dear Editor,

The World Health Organization considers obesity as one of the most serious global health problems with a negative feedback on mother and fetus. Obesity represents an imbalance between energy intake from food and energy output expended as physical and metabolic activity.^[1] The effect of maternal obesity on birth outcomes is of great public health important. Body mass index (BMI) above the normal range is associated with a number of adverse reproductive health outcomes.^[2] Infertility, ovulation dysfunction, increase risk of first trimester abortion and recurrent miscarriage^[3] also obesity causes complication during pregnancy: gestational diabetes, pregnancy-induced hypertension and preeclampsia, birth defects, large for gestational age or macrosomia (>4500 g) cesarean sections prolonged labor, and recently, postpartum hemorrhage^[4] has been associated with maternal. Several studies have been shown an increased risk for birth defects associated with maternal obesity.^[5,6]

Our surveillance system uses active case finding among records of birth in Al-Hilla Teaching Hospital, Babylon province. The affected infants that have been identified are live birth, stillbirth, preterm labor and abortion more than 20 weeks of gestation. To be eligible for inclusion as either a case or a control, infants had to be born between April 2018 and November 2018. The control are infant's without any congenital abnormalities. We collected 60 mothers for the control and 60 mothers for the case.

All the mothers of case and control infants complete an interview with questions on age, maternal health, medication use, pregnancy history and fertility, demographics, family history, nutrition, occupational and environmental exposures, and tobacco use. Mother's weight and height also had been recorded for calculation of BMI.

Furthermore, we completed with each woman a full investigations; Blood checked for sugar (to excluded the possibility of diabetes (fasting and random). Test for Toxoplasmosis using serological test detects Antibodies IgM, for Cytomegalovirus IgM Ag and Rubella IgM to exclude the possibility of perinatal infection (if pregnant mother with positive test excluded).

To exclude the possibility of perinatal infection, all the mothers of age <18 years or more than 35 years were excluded. The fetus or the neonate examined by a pediatrician to catch any possible recognized chromosomal or hereditary abnormality is to be excluded from the study.

Data were analyzed using SPSS version 17 Chi² test estimation of odd ratios (ORs) from stratified analysis was obtained and presented in the table of this study. OR of ≥ 1.5 revealed that

defect had an elevated risk. 95% confidence intervals were calculated using the Mantel-Haenszel method.

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patient verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee.

Of 60 normal mothers (BMI 18.5–24.9 kg/m²), there were 43 average, 10 overweight, and 7 obese. The collected data of this study were analyzed, and the results was that, Chi² test (significant ($P \leq 0.01$)) the comparison of BMI between control and cases, is that there were significant differences between the two groups of study, 71.67% of control group women had (BMI 18.5–24.9) in comparison with (48.57%) of case group, on the other hand, 28.33% had BMI $25 \geq 30$ in comparison with 51.43%.

Table 1 demonstrates the comparison of infant abnormalities between control, average weight women, and obese women; there was more infants with a neural tube defect (33.33%) in obese mothers, in obese mothers, especially spina bifida (OR: 3.1, 95% CI: 1.4–11.6) and anencephaly (OR: 2.9, 95% CI: 0.7–11.4) in comparison to average weight women. Also obese women were more likely to have an infant with hydrocephalic defect (OR: 3.0, 95% CI: 1.4–8.2) in comparison with average weight women in addition, overweight women have an infant with defect, such as meningocele (OR: 2.2, 95% CI: 1.1–4.6), spina bifida (OR: 2.1, 95% CI: 1.3–7.2), meningocele and hydrocephaly (OR: 2.1, 95% CI: 1.1–3.0), hydrocephaly (OR: 1.7; 95% CI: 0.8–6.1), meningocele and anencephaly (OR: 1.6; 95% CI: 0.6–3.7) and anencephaly (OR: 1.5; 95% CI: 0.6–5.9) multiple abnormalities were also observed to be increased significantly in obese and overweight mothers (OR: 2.0; 95% CI 1.1–3.6) and (OR: 2.0; 95% CI 1.1–4.4) respectively in comparison with normal weight.

Our results showed that the risk estimate of OR: 3.1 for spina bifida in obese mothers is higher than that of Waller *et al.*^[7] (OR: 2.6), but it was approximate to the results of Watkins *et al.*^[8] (OR: 3.5), but higher than that of Waller *et al.*^[7] (OR: 2.6). Furthermore, overweight mothers were at significantly increased odd of a pregnancy affected by spina bifida compared with mother of normal BMI in our study (OR: 2.1). This result was much larger than finding of Watkins *et al.* (OR: 1.5).^[8]

Also, estimate of (OR: 2.9) anencephaly was higher than (OR: 1.12) previously reported by Anderson *et al.*^[9] Watkins *et al.*^[8] did not observe an elevated risk for orofacial clefts (OR: 1.29), and this in agreement with our results (OR: 1.4), since

Table 1: Odds ratio* for study cases by body mass index category (referent=average weight (body mass index 18.5-24.9))

Variables	Total	Average (control) (BMI 18.5-24.9), n	Overweight (BMI 25-29.9)		Obese (BMI >30)	
			n	OR (95% CI)	n	OR (95% CI)
Cases	60	30	22		14	
Hydrocephaly	14	7	3	1.7 (0.8-6.1)	2	3.0 (1.4-8.2)
Spina bifida	7	4	1	2.1 (1.3-7.2)	2	3.1 (1.4-11.6)
Anencephaly	10	4	3	1.5 (0.6-5.9)	2	2.9 (0.7-11.4)
Meningocele and anencephaly	1	0	1	1.6 (0.6-3.7)	0	-
Meningocele and hydrocephaly	1	0	1	2.1 (1.1-3.0)	0	-
Cleft lip and cleft palate	3	1	2	1.4 (0.3-3.4)	0	-
Skin abnormalities	3	1	0	-	2	1.1 (0.6-3.9)
Intestinal obstruction	1	0	1	1.2 (0.1-7.4)	0	-
Limb abnormalities	9	5	3	1.0 (0.5-1.9)	1	0.9 (0.3-1.5)
Genital abnormalities	1	0	1	1.3 (0.7-3.3)	0	-
Meningocele	5	3	2	2.2 (1.1-4.6)	0	-
Umbilical hernia	1	0	1	0.6 (0.5-4.1)	0	-
Polycystic kid	3	0	1	1.2 (0.6-3.8)	2	1.2 (0.6-3.1)
Multiple abnormalities	11	5	2	2.0 (1.1-4.4)	3	2.0 (1.1-3.6)

*OR of >1.5 revealed that defect had an elevated risk. OR: Odds ratio, CI: Confidence interval, BMI: Body mass index

we reported no risk elevation for cleft lip and cleft palate in mothers who were overweight, although the OR was close to significance.

In this investigation, there was no association between either maternal overweight or obesity and the risk factor of pregnancy affected by skin abnormalities, intestinal obstruction, limb abnormalities, genital abnormalities, umbilical hernia, and polycystic kidney. The mechanism for the observed association between obesity and birth defects is not known, but several possible explanations have been proposed. One explanation might be that obese women have metabolic alterations, such as hyperglycemia or elevated insulin or estrogen levels, that increase their risk for birth defects. Hyperinsulinemia^[10] has been shown to be an independent risk factor for neural tube defects, but even after adjustment for hyperinsulinemia, obesity continued to be a modest risk factor.^[7] Another explanation is that women who are obese might have diabetes, a known risk factor for birth defects.^[4]

In previous studies, the relation between obesity and neural tube defects persisted, even when women with known diabetes were excluded or when adjustment was made for diabetes; however, some women with diabetes might be unrecognized. Women who are obese also might have nutritional deficits, resulting from dieting behaviors or poor-quality diets,^[11] that increase their risk for congenital anomalies. Previous studies have shown that multivitamins and folic acid intake are similar among obese and nonobese women; however, other nutrients, currently not recognized as causing birth defects, might play a role. Another explanation is that women who are obese might have an increased requirement for certain nutrients (e.g., folic acid) known to be protective against birth defects. The study by Werler *et al.*^[12] provides some evidence for this hypothesis: the reduction in neural tube defect risk typically associated with folic acid was not observed among

heavier women. Folic acid requirements are mentioned to be doubled during pregnancy,^[9] while 400 mcg of folic acid can reduce spina bifida birth defects by about 40%; 1000 mcg reduces birth defects by about 50%.

Our study showed that obese women are at greater risk of having a child with specific major congenital anomalies, especially neural tube defects given the fact that the number of overweight and obese women is rising.

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Conflicts of interest

There are no conflicts of interest.

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