RISK FACTORS OF FETAL MACROSOMIA : ROLE OF MATERNAL NUTRITION

Walid Denguezli, Raja Faleh, Anissa Fessi, Alaeddine Yassine, Awatef Hajjaji, Hayett Laajili, Mohamed Sakouhi.

Department of Obstetric and Gynaecology. University Hospital Fattouma Bourguiba, Monastir, Tunisia.

W. Denguezli, R. Faleh , A. Fessi, A. Yassine, A. Hajjaji, H. Laajili, M. Sakouhi.

FACTEURS DE RISQUE FOETAL MACROSOMÍA: RÔLE DE LA NUTRITION MATERNELLE

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RÉSUMÉ

But : Evaluer effet de l'apport alimentaire maternel en fin de grossesse sur le risque de survenue de macrosomie fœtale.

Méthode : il s'agit d'une enquête alimentaire réalisée auprès de 350 femmes enceintes à terme de grossesse monofœtale, de déroulement normal. Les femmes ont répondu à un questionnaire comportant des informations relatives aux apports quantitatifs selon la méthode de rappel des 24 heures.

Résultats : la fréquence de la macrosomie fœtale était de 15.8 % (n=52). Les apports quotidiens moyens en micronutriments étaient significativement plus élevés dans le groupe macrosomie par rapport au groupe contrôle. L'obésité maternelle avant la grossesse et l'antécédent de macrosomie fœtale étaient les facteurs épidémiologiques maternels les plus corrélés au risque de macrosomie fœtale sans atteindre le seuil de signification statistique. Un apport calorique quotidien supérieur à 2600 Kcal/j, un apport protéique supérieur à 90g/j, un apport lipidique supérieur à 70g/j étaient accompagnés d'une augmentation non significative du risque de macrosomie fœtale. Cependant, après analyse multivariée aucun de ces apports n'était significativement corrélé au risque de macrosomie fœtale.

Conclusion : les apports alimentaires maternels en en fin de grossesse ne semblent pas être un facteur déterminant de la survenue de macrosomie fœtale comparé à l'obésité maternelle avant la grossesse.

MOTS-CLÉS

Alimentation -Grossesse –macrosomie fœtale

SUMMARY

Aim : To assess the effect of maternal diet during pregnancy on the risk of delivering a large for gestational baby (macrosome).

Methods: A food intake survey of 350 healthy pregnant Tunisian women, 52 in group macrosomia and 298 in group control. Only term (≥ 37 completed Weeks of gestation) infants were included. All women in the study group completed food frequency questionnaires on their diet in the last 24 hours before delivery.

Results: Frequency of foetal macrosomia was 15.8 % (n=52). Pregravid maternal BMI > 30(OR= 3,06[1,51-6,17]), prolonged term of pregnancy(> 41weeks of gestation) (OR=2,49[1,04-5,88]) and the antecedent of a macrosomic delivery (OR=6,53[2,89-14,74]) were significantly associated with the risk of fetal macrosomia. The mean daily total energetic intakes, protein intakes and carbohydrate intakes were significantly higher in the macrosomia group than in the control group. However, with multivariate analysis after adjustment for term and Pregravid BMI, no significant correlation was found between nutrient intakes and risk of fetal macrosomia.

Conclusion: Maternal food intakes in the end of pregnancy are not a significant determinant of fetal macrosomia compared to maternal BMI, and term of pregnancy.

KEY-WORDS

Nutrition- Pregnancy-Fetal macrosomia.

Foetal macrosomia is often defined using a crude birth weight, with varying cut-off points. Four kilograms is used most frequently, which approximates to the 90th centile at 40 weeks of gestation. Macrosomic infant are at increased risk of shoulder dystocia, brachial plexus injury, skeletal injuries, meconium aspiration, perinatal asphyxia and perinatal foetal death [1,2]. Risk factors of foetal macrosomia are numerous and intricate, of which gestational age is the most important. Therefore, centile birth weight controlled for gestation may be more appropriate when studying foetal growth or outcomes where gestational age has a significant confounding effect. Other risk factors of foetal macrosomia were identified, such as maternal pre-gravid weight, height, weight gain during pregnancy, age and parity. All these factors were positively associated with birth weight [3]. Numerous studies have shown the importance of maternal nutrition during pregnancy and its influence on foetal growth [4,5]. However, controversy persists regarding the role of maternal nutrition during the end of pregnancy as a determinant of foetal macrosomia, especially countries with poor resources [6]. In more recent years, we have experienced a nutritional transition, as result of developmental progress, which has been characterised by a rise in a rate of obesity and sedentarily.

The objective of this study was to assess if maternal nutrition during the end of pregnancy is a significant determinant of foetal macrosomia.

MATERIAL AND METHODS

The study consisted in a food intake survey lead in 350 Tunisian pregnant women at term, in the Department of Obstetric and Gynaecology of Monastir (Tunisia), during a five month period (October 2002-February 2003). All pregnancies were single, with delivery at term at term (≥ 37 Weeks of gestation). Foetal macrosomia was defined as a birth weight superior to the 90th percentile in the curve of "Lubchenco ". We excluded from this study all women presenting one or more fœto-maternal risk factor, particularly, gestational or pregravid diabetes, antecedent of preeclampsia or gestational hypertension, all known maternal thyroids pathology and multiple pregnancies. After consent, all women answered a food questionnaire based on «24-hour – recall" method. Information collected was treated with "Bilnut 2.0" software adapted to Tunisian food. It converts food daily intakes in proportion of micronutrients (Carbohydrate; fats, proteins, salts and vitamins…). The studied population was subdivided in two groups: «macrosomia group» (GM): composed with women that delivered a macrosomic newborn and "control group" (GC) composed by women that delivered a normal weight newborn. Sources of data used for this study were: the cross-examination of women's and obstetric files. Compilation of data was made before delivery; by an investigator physician that was blinded to the scan and the clinically estimated fœtal weight. A screening for gestational diabetes was performed for all women delivering macrosomic infant. Assessment of the women's food intakes diaries was based on the French Recommended Dietary Allowance (RDA) (ANC 2001) [7]. All of the women's epidemiological parameters (age, parity, antecedents,..) and food intake parameters during the last 24 hours preceding delivery were recorded. Different food intakes were correlated to newborn birth weight. Statistical analysis has been achieved by SPSS 11.0 software. Maternal and infant charts were reviewed for maternal and neonatal outcomes, demographic variables included parity, pre-gravid body mass index (BMI), delivery of an macrosomic infant (defined as birth weight ≥ 4000 g), or family history of diabetes. Mainly outcomes included correlation between quantitative maternal food intakes, birth weight and risk of foetal macrosomia. Statistical data was calculated by c^2 for nominal analysis and stepwise logistic regression for multivariate analysis. The difference between groups was considered as significant if $p<0,05$.

RESULTS

During study period, 350 women were included, they delivered of 350 newborns, of which 52 (15.8%) were macrosomic. All other newborns (298) were of normal birth weight (group control). Table I shows maternal characteristics by birth weight category. Mean maternal parity, term at delivery, pre-gravid weight and BMI were significantly higher in GM than in GC. (Table I).

Table 1 : Epidemiologic characteristics in study groups

PARAMETRES	GM	GC	P
Age (Year)*	29.85 ± 4.61	28.68 ± 5.48	0.17
Parity*	2.71± 1.46	2.23 ± 1.15	0.008
Term (Wg)*	40.44 ± 1.25	39.52 ± 1.41	< 0.001
Pregravid weight (Kg)*	71.69 ± 15.24	63.9 ± 11.20	< 0.01
BMI (Kg/m^2)*	28.16 ± 5.33	25.45 ± 4.2	< 0.01

(*) : Results are expressed as mean and standard deviation. BMI: Body mass index. (Wg) : Week of gestation.

We noted a high frequency of obesity and weigh excess in our population. Indeed, 50% of study population had a pregravid BMI ≥ 25 kg/m2 (Table II). This study confirmed the high correlation between birth weight and obesity (BMI ≥ 30) (Table II). Inversely, a BMI < 25 was associated with a significant reduction in foetal macrosomia risk (OR = 0.55-IC 95% [0.26-0.97]) (Table II). In contrast, maternal age was not significantly associated with foetal macrosomia. Antecedent of foetal macrosomia was the most powerful determinant factor of foetal macrosomia. Epidemiologic and anthropometric maternal characteristics in groups and their effect on foetal weight are represented in table II.

Mean total daily caloric intakes (2701 ± 622 Kcal/day) correspond to the recommended allowance (ANC= 2600Kcal/day). Furthermore, most of study group (62,9%) had a hypercaloric ration (more than 2600Kcal/j).

The average protein intakes were 90,8 ± 20,1 g/day (1,2 g/kg/day) (19,7- 137,6 g/day). Average lipids intakes were 75,9 ± 29,8 g/day (11,7 to 174,4 g/day). Mean carbohydrate daily intakes were 413,6 ± 105,7 g/day. Characteristics of maternal nutrient intakes composition by groups are represented in

Tables III and IV. Our study showed that when recommended dietary allowances are overtaken, risk of foetal macrosomia was increased (Table III). Our results showed that only carbohydrate intakes were significantly correlated to foetal macrosomia (OR=10,3 IC [1,48-204,8]).

Table 3 : Diary dietary intakes in study groups

Nutritional parameter (*)	Group Macrosomia	Group Control	P
Mean total Energy (Kcal/day)	3124,9 ± 403	2626,98 ± 624,63	<0,001
Mean Protein intakes (g/day)	103,18 ± 17,12	88,68 ± 19,78	<0,001
Mean Fat intakes (g/day)	79,03 ± 24,75	75,41 ± 30,56	0,41
Mean glucidic intakes (g/day)	500,15 ± 75,35	398,51 ± 103,13	<0,001

(*): Results are expressed as mean ± standard deviation.

However, logistic regression analysis, with and without adjustment for the pregravid BMI, parity and term, didn't show any significant correlation with birth weight. (Table V).

Table 4 : comparison of Nutrient intakes in study groups

Nutritional Parameter (ANC 2001) [a]		Group Macrosomia	Group Control	OR –IC 95%
TDEI[b] (Kcal/day)	≥ 2600	38	172	1,83 [0,91-3,72]
	< 2600	14	116	
Proteins(mg/kg/day)	≥ 0,9	47	245	1,87 [0,78-4,49]
	< 0,9	5	53	
Fats (g/day)	≥ 70	34	154	1,77 [0,92-3,42]
	<70	18	144	
Glucids (g/day)	≥ 300mg	51	248	10,3 [1,48-204,8]*
	< 300	1	50	

(a) : Values based on the French recommended allowance « ANC 2001 ».
(b) : Total daily energetic intakes.

Table 5 : Effect of Nutrient intakes on risk of Macrosomia.
(Multiple logistic regression analysis with and without adjustment for Term, parity and BMI)

Nutrient parameter	Without Adjustment		After Adjustment	
	OR	OR - IC 95%	OR	OR-IC 95%
Total energy intakes	1,045	[0,96-1,13]	1,04	[0,96-1,12]
Protein intakes	0,85	[0,60-1,19]	0,40	[0,64-1,20]
Glucidic intakes	0,84	[0,60-1,18]	0,86	[0,63-1,18]
Fat intakes	0,67	[0,31-1,42]	0,33	[0,35-1,41]
SFGA [1]	0,96	[0,89-1,04]	1,024	[0,95-1,10]
Apport en MIF A [2]	1,03	[0,96-1,10]	0,98	[0,91-1,05]

Table 2 : Maternal epidemiologic characteristics and foetal macrosomia

MATERNAL CHARACTERISTIC		GROUP MACROSOMIA (n)	GROUP MACROSOMIA (%)	GROUP CONTROL (n)	GROUP CONTROL (%)	OR (IC) 95%
Age (Year)	<19	0	0	1		-
	19 -35	47	15.3	259	84.6	1.42 [0.5-432]
	> 35	5	11.62	38	88.37	0.73 [0.24-2.07]
Parity	1	9	8.9	92	91.1	0.47 [0.2 -1.05]
	2 -3	30	15.5	164	84.5	1.11 [0.59-2.11]
	> 3	13	23.6	42	76.4	2.03 [0.94 -4.34]
Pregravid BMI (Kg/m²)	< 25	17	10.36	147	89.6	0.55 [0.26 -0.97]*
	25-30	17	14.9	107	85.1	0.87 [0.44 -1.69]
	> 30	18	29	44	71.7	3.06 [1.51 -6.17]*
Term (Wg)37	- 41	42	12.5	272	87.5	0.4 [0.17 -0.96]*
	> 41	10	27.7	26	72.2	
Antecedent of Foetal macrosomia						
	Yes	16	10,3	19	5,4	6,53[2,89-14,74]*
	No	36	4,6	279	79,7	

DISCUSSION

This study didn't find any significant correlation between fœtal macrosomia and maternal food intakes in the last period of pregnancy. However, it showed a notably increased risk for fœtal macrosomia when the carbohydrate intakes passed the RDA (300 g /day). It confirms the results of a first Tunisian study conducted in 1990 by Gaïgi et al. that showed a strong correlation between maternal carbohydrate intakes and birth weight [6]. Our results showed a positive correlation between maternal intakes and fœtal weight; however this significant effect disappears after adjustment for confounding factors such as parity, term of pregnancy and pregravid BMI (Table V). In the literature, the results of studies are controversial. These studies were conducted essentially in developed countries that have not necessarily the same habits that ours. In Tunisian pregnant population women, Gaigi et al. (1990) did not findany correlation with birth weight [6]. These suggestions were confirmed by Mathews et al. Who could not find any correlation of birth weight with maternal protein intakes, in both first and third trimester of pregnancy [5]. Kramer et al. (1998) showed that the quality of maternal intakes was more important than quantitative [8]. However, they noticed that women's consumption of a weak quantity of retinol derivatives were accompanied of a medium increase of 160g in birth weight. Therefore, it is admitted that women with excessive caloric intakes could have an adequate or even excessive weight gain during pregnancy, but there was an increase in neonatal morbidity and mortality [9]

The effect of maternal nutrition on birth weight seems to act by modification of intrauterine environment in witch insulin seems to play an essential role. Indeed, relationships between rates of umbilical insulinemia and birth weights have been noted [10]. This is especially true in diabetic woman for which it was demonstrated that a strict control of maternal glycaemia permitted a significant reduction in the risk of foetal macrosomia [11].

It is well established that placental transport of glucose is controlled by the level of maternal glycaemia. Indeed, an increase of the glucose transfer from mother toward fœtus has been observed in an experimental model of insulinoprive diabetes [12]. In analogous, applied conditions, an increase of the expression of the gene of the placental transporters (GLUT3) was correlated to maternal glycaemia. However, insulinemia variations were without effect on expression of these transporters [13]. The role of GLUT3 in the increase of the glucose placental flow of and foetal macrosomia is suggested. Our study confirms these results; it showed a 10-folds increased risk of fœtal macrosomia if carbohydrate maternal intakes passed the RDA. In fact, glucose would be one of many substrata's: such as amino acids, triglycerides and free fatty acids who cross the placenta and could modulate insulin secretion [13].

Leptine is a major hormone produced by adipocytes; it plays an important role in regulation of post native weight [14]. The existence of correlation between umbilical concentration of leptine and birth weight and the umbilical concentration of insulin [14,15] illustrates its role in fœtal growth. The leptine is produced by placenta early during pregnancy at elevated rates, comparable to those of the adipose tissue [16, 17]. Because of the ambient, fœtal and maternal hyperinsulinism, a regulation of the leptine placental production by insulin is considered.

Our study showed an independent and significant effect of maternal factors such as maternal BMI and term of pregnancy on risk of fœtal macrosomia; this can be due to the high prevalence of obesity in our population. Indeed, all authors agree on the major importance of pre-gravid weight and the hold of weight on the foetal weight [18]. Currently, it is estimated to 30% the degree of variance of fœtal weight due to these factors [19].

The genetic factor is less important; several authors noticed the importance of this factor and the interrelationship between maternal birth weight, and size with birth weight of its child [19]. The phenomenon of the parental print, recently described, illustrates this effect well. It consists in a mechanism regulation of expression of indispensable genes to the fœtal development and placental transfer of micronutrients. According to this theory, Haig et al. [20] suggested that paternal genes assure the promotion of the fœtal growth whereas, maternal genes acts against this growth. Our study is criticisable because it doesn't take into account the maternal food in the first trimester of pregnancy. First trimester depends largely of the situations of food unbalance at the pregnant women especially occur at those excluding some families of food or belonging to underprivileged socioeconomic classes.

RÉFÉRENCES

1. Ehrenberg HM, mercer BM, Catalano PM. The influence of obesity and diabetes on prevalence of macrosomia. Am J Obstet Gyneco 2004;191:964-968
2. Kolderup LB, Laros RK Jr, Musci TJ: Incidence of persistent birth injury in macrosomic infants: association with mode of delivery. Am J Obstet Gynecol 1997; 177:37–41
3. Lepercq J, Timist J, Hauguel-deMouzon S. Etiopathogénie de la macrosomie fœtale. J Gynecol Obst Biol Rep 2000; 29 (s1):6-1
4. Rao S, Yajnik CS, Kanade A, Fall CHD, Margetts BM, Jackson AA, Shier R, Joshi S, Rege S, Lubree H and Desai B. Intake of Micronutrient-rich foods in rural indian mothers is associated with the size of their Babies at birth: Pune Maternal Nutrition Study. J Nutr. 2001; 131 : 1217–1224
5. Mathews F, Yudkin P, Neil A. Influence of maternal nutrition on outcome of pregnancy: prospective cohort study. BMJ. 1999; 319 : 339-43
6. Gaïgi SS, Jallouli K, Doghri T, Gaïgi S. Alimentation de la femme enceinte et poids de l'enfant à la naissance. Tunis Medicale 1990; 68 : 459-462.
7. Martin A. Besoins et apports nutritionnels conseillés Besoins nutritionnels au cours de la grossesse et de la lactation .Cah Nutr Diét 2001; 36 (hors série1):7-13
8. Kramer MS. Maternal nutrition, pregnancy outcome and public health policy. CMAJ. 1998; 159 : 663-5.

9. Lepercq J , Boileau P. Physiologie de la croissance fœtale. EMC-Gynécologie Obstétrique 2 (2005) 199–208.
10. Bernstein IM, Goran MI, Copeland KC. Maternal insulin sensitivity and cord blood peptides: relationships to neonatal size at birth. Am J Obstet Gynecol 1997; 90: 780-3.
11. Langer O, Mazze R. The relationship between large-for-gestational-age infants and glycemic control in women with gestational diabetes. Am J Obstet Gynecol 1988; 159: 1478-83.
12. Boileau P, Mrejen C, Girard J, Hauguel-de Mouzon S. Over expression of GLUT3 placental glucose transporter in diabetic rats. J Clin Invest 1995; 96: 309-17.
13. Giudice LC, de Zegher F, Gargosky SE, Dsupin BA, de lasFuentes L, Crystal RA, Hintz RL, Rosenfeld RG. Insulin-like growth factors and their binding proteins in the term and preterm human fetus and neonate with normal and extremes of intrauterine growth. J Clin Endocrinol Metab 1995; 80: 1548-55
14. Girard J. Is leptin the link between obesity and insulin resistance? Diabetes Metab 1997; 23: 16-24.
15. Lepercq J, Lahlou N, Timsit J, Girard J, Hauguel-de Mouzon S. Macrosomia revisited: Ponderal index and leptin delineate subtypes of fetal overgrowth. Am J Obstet Gynecol 1999.
16. Lepercq J, Cauzac M, Lahlou N, Timsit J, Girard J, Auwerx Hauguel-de Mouzon S. Overexpression of placental leptin diabetic pregnancies : a critical role for insulin. Diabetes 1998 47: 847-50.
17. Masuzaki H, Ogawa Y, Sagawa N, et al. Nonadipose tissue production of leptin : leptin as a novel placenta-derived hormone in humans. Nature Med 1997; 3: 1029-33.
18. Ducarme G, Rodrigues A, Aissaoui F, Davitian C, Pharisien I, M. Uzan. Grossesse des patientes obèses : quels risques faut-il craindre ?. Gyn Obstet Fert 2007 ;35 : 19–24
19. Stephenson T, Symonds ME. Maternal nutrition as a determinant of birth weight. Arch. Dis. Child. Fetal Neonatal 2002 ; 86 :4-6
20. Moore T, Haig D. Genomic imprinting in mammalian development: a parental tug-of-war. Trends Genet 1991;7:45–9.