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Determinants for Macrosomia in a Mediterranean Island community

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Abstract

Macrosomia has been associated with patient socio-biological determinants and poses increased perinatal risks to mother and child. The study set out to identify these determinants and assess the risk in a high NIDDM prevalence population. Maternal biological characteristics and obstetric outcomes of 988 infants weighing more than 4000 gm were statistically compared to similar parameters of 15653 infants of lower birth weight. Macrosomia appeared to be commoner in the older obese previously diabetic woman aged more than 30 years who had at least one previous pregnancy or miscarriage. Hypertensive disease was a negative correlate. The macrosomic infant was more likely to require an operative intervention for delivery. The delivery was similarly more likely to be complicated by shoulder dystocia. The tendency for macrosomia appears to be related to maternal insulin-resistance metabolic syndrome; while the infant size predisposed to definite intrapartum problems. Effective intervention therapies to combat excessive fetal growth need to be identified and introduced in clinical practice to prevent the long-term consequences of macrosomia to the infant.

Keywords: *macrosomia, pregnancy, outcome, complications*

Introduction

A macrosomic infant is generally defined as one with a birth weight greater than the 90th centile for that population, a definition that includes all infants born with a birth weight greater than 4000 gm. The incidence of fetal macrosomia varies from one community to another and furthermore has shown temporal changes in the same community. The different incidence patterns suggest that patient socio-biological factors may play a determinant role in the development of macrosomia. Macrosomic babies have been associated with maternal diabetes and obesity; while the larger size of the infant imposes greater risks of birth trauma to the infant and the necessity of operative intervention to achieve a safe delivery.[1,2,3]

The Maltese population comprises a small island community in the Central Mediterranean with a high prevalence of maturity onset diabetes mellitus reflected in a high prevalence of gestational glucose intolerance.[4,5] The incidence of fetal macrosomia, defined as a birth weight greater than 4000 gm, in this population has been reported to have decreased from 11.5% in 1983-86 to 5.9% in 1999-2002. While this fall may partly be attributed to an increase in the obstetric intervention rate with earlier timing of delivery, changes in the socio-biological characteristics of the mothers such as age at delivery patterns may also have played a determinant role.[6] The aim of the study was to identify the maternal factors that may predispose towards fetal macrosomia and to study the outcome of these fetuses.

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Material & methods

The study reviewed the medical data records of all women delivering in the Maltese Islands during 1999-2002 [n = 16,413 maternities resulting in 16,641 births]. The medical data was made available by the National Obstetric Information System managed by the Department of Health Information [Malta]. The medical records revealed a total of 988 infants born with a birth weight equal to or greater than 4000 gm divisible into 861 infants weighing 4000-4499 gm and 127 infants weighing >4500 gm. The maternal biological characteristics and obstetric outcomes of these infants were compared between each group and with those of infants weighing less than 4000 gm. The latter group include macrosomic infants for their gestational age but less than 4000 gm. Further comparison was made with the outcome parameters of the remaining background population delivering during the same period who presumably had a birth weight less than 4000 gm. The data analysis was carried out using SPSS package with statistical significance being tested using the Chi Square test generally using a 3-table comparison unless specifically indicated. A probability value of <0.05 was taken to represent a significant correlation.

Results

A number of maternal biological factors were shown to relate statistically to the likelihood for delivering a macrosomic infant weighing >4000 gm (Table 1). The older patient aged more than 30 years was statistically ($p<0.0001$) more likely to have a high birth weight infant when compared to women aged less than 30 years. The multiparous patient who had at least one previous pregnancy ($p<0.0001$) or miscarriage ($p=0.04$) was similarly statistically more likely to deliver a macrosomic infant. While a relationship was suggested

Table 1: Maternal biological determinants in 16413 pregnancies in Malta

Maternal Parameters	Infant Birth Weight					
	<4000 gm		4000-4499gm		>4500 gm	
Maternal Age						
<20 years	912	5.9%	41	4.8%	3	2.4%
20-29 years	9118	58.7%	457	53.3%	54	42.9%
30-39 years	5105	32.9%	333	38.8%	60	47.6%
>40 years	402	2.6%	26	3.0%	9	7.1%
*p<0.0001**	*n=15537*		*n=857*		*n=126*	
Previous miscarriages						
M 1+	572	15.6%	154	17.9%	27	21.4%
P=0.08	*Data for 2002 only*					
*<4.0 vs >4.0 kg p=0.04**	*n=3660*		*n=861*		*n=126*	
Previous Live Births						
P 1+	7459	49.8%	515	59.9%	90	70.9%
P=0.15						
*<4.0 vs >4.0 kg p<0.0001**	*n=14988*		*n=860*		*n=127*	
Previous Perinatal loss						
PND 1+			15	1.7%	3	2.4%
4.0-4.5 vs >4.5 kg p=0.90	*Data unavailable*		*n=861*		*n=127*	
Previous Cesarean						
LSCS 1+			90	10.5%	19	15.0%
4.0-4.5 vs >4.5 kg p=0.18	*Data unavailable*		*n=859*		*n=127*	
Body Mass Index [pre-pregnancy]						
<20			13	1.6%	1	0.9%
20-24			214	26.9%	17	14.9%
25-29			301	37.9%	41	36.0%
30-34			168	21.1%	35	30.7%
35-39			77	9.7%	13	11.4%
>40			22	2.8%	7	6.1%
*4.0-4.5 vs >4.5 kg p=0.02**	*Data unavailable*		*n=795*		*n=114*	

Table 2: Medical and Antenatal determinants of macrosomic and non-macrosomic infants in Malta

Medical & Antenatal	Infant Birth Weight					
Parameters	<4000 gm		4000-4499gm		>4500 gm	
Diabetes Mellitus						
GDM [*WHO criteria*]	346	2.2%	35	4.1%	13	10.2%
Pre-existing DM	44	0.3%	10	1.2%	3	2.4%
*p<0.0001**	*n=15425*		*n=861*		*n=127*	
Hypertensive disease						
Yes	1048	6.8%	40	4.7%	8	6.3%
p=0.07	*n=15454*		*n=861*		*n=127*	
*<4.0 vs >4.0 kg p=0.02**						
APH						
Yes	382	2.5%	19	2.2%	5	3.9%
p=0.50	*n=15454*		*n=861*		*n=127*	
<4.0 vs >4.0 kg p=0.96						
Artificial reproduction						
Yes	117	1.1%	10	1.2%	1	0.8%
p=0.43	*n=15402*		*n=861*		*n=127*	
<4.0 vs >4.0 kg p=0.30						

Table 3: Intrapartum outcomes of 16641 births occurring in Malta in the years 1999- 2002

Intrapartum	Infant Birth Weight					
Parameters	<4000 gm		4000-4499gm		>4500 gm	
Type of delivery						
Elective CS	2036	13.0%	98	11.4%	23	18.1%
Emergency CS	1660	10.6%	114	13.2%	19	15.0%
Operative vaginal	590	3.8%	49	5.7%	7	5.5%
*P<0.0001**	*n=15647*		*n=861*		*n=127*	
Trauma in vaginal deliveries						
Extended trauma			252	29.3%	28	22.0%
4.0-4.5 vs >4.5 kg p=0.15	*Data unavailable*		*n=861*		*n=127*	
Retained Placenta						
Yes			7	0.8%	2	1.6%
4.0-4.5 vs >4.5 kg p=0.74	*Data unavailable*		*n=861*		*n=127*	
Shoulder dystocia						
Yes	47	0.3%	13	1.5%	17	13.4%
*P<0.0001**	*n=15647*		*n=859*		*n=127*	

Table 4: Infant characteristics and outcome of 16641 pregnancies in Malta during the years 1999-2002

Infant	Infant Birth Weight					
Parameters	<4000 gm		4000-4499gm		>4500 gm	
Fetal sex						
Female	7742	49.5%	320	37.2%	43	33.9%
Male	7906	50.5%	541	62.8%	84	66.1%
P=0.17	*n=15648*		*n=861*		*n=127*	
*<4.0 vs >4.0 kg p<0.0001**						
Apgar score @ 5 min						
Score <=6	189	1.2%	9	1.1%	2	1.6%
P=0.85	*n=15653*		*n=861*		*n=127*	
Infant outcome						
Perinatal death	148	1.2%	2	0.2%	1	0.8%
P=0.11	*n=15653*		*n=861*		*n=127*	
<4.0 vs >4.0 kg p=0.06						
Infant feeding						
Bottle feeding	7781	51.0%	329	38.9%	66	53.2%
Breast feeding only	5566	36.5%	375	44.4%	32	25.8%
Mixed feeding	1919	12.6%	141	16.7%	26	21.0%
*P=0.0009**	*n=15266*		*n=845*		*n=124*	

for higher birth weight infants in mothers who had a previous perinatal loss or a pregnancy delivered by a previous Cesarean section, these parameters did not show statistical significance. A statistically significant relationship was shown between increasing infant birth weight and maternal Body Mass Index (p=0.02).

Maternal medical and antenatal problems also apparently influenced the determination of the eventual infant's birth weight (Table 2). The only positive statistically significant determinant (p<0.0001) identified was the presence of pre-existing diabetes mellitus (IDDM and NIDDM) and gestational diabetes as defined by the WHO criteria.[7] Hypertensive disease, whether gestational or pre-existing, appeared to be a negative statistical (p=0.02) co-relate so that the presence of the disorder predisposed towards lower infant birth weight. There did not appear to be any statistical relationships with a history of antepartum haemorrhage (p=0.96), accidental or placenta praevia, and the necessity for ovulation induction intervention to achieve a pregnancy [p=0.30]. There were no cases of multiple pregnancies among the macrosomic group.

Infant size showed a significant effect on the intrapartum outcome [Table 3]. Macrosomic infants were statistically (p<0.0001) more likely to require an operative intervention in

the form of a Cesarean section or an operative vaginal delivery. Because of the increased use of Cesarean section for macrosomic infants, delivery trauma did not show any statistical ($p=0.15$) increase with increasing birth weight. The second stage of labour appeared to be increasingly complicated in the presence of macrosomic infants with an increasing predisposition ($p<0.0001$) towards shoulder dystocia in spite of the increasing use of Cesarean section. Retained placenta appeared to be more likely in the presence of macrosomic infants though the difference showed no statistical significance ($p=0.74$).

Macrosomic infants were statistically ($p<0.0001$) more likely to be male rather than female. The perinatal outcome did not appear to be adversely influenced by infant birth weight showing no statistical differences in the rates of low Apgar scores at 5 minutes ($p=0.85$) and perinatal deaths ($p=0.06$). (Table 4). None of the infants suffered from respiratory distress, seizures or significant hyperbilirubinaemia in the perinatal period. Infant feeding appeared to be statistically dependent on infant body weight, so that the very large infants weighing >4500 gm were more likely to be given artificial feeding as a primary form of feeding or as an adjuvant. More infants weighing 4000-4499 gm appeared to be breast-fed at the time of discharge from hospital.

Discussion

The observed decrease in the incidence of macrosomia defined as a birth weight >4 000 gm in the Maltese population over the last 15 years has suggested a possible socio-biological predisposing factor influencing fetal growth. The fall in macrosomia rate in the Maltese population contrasts with the secular trends in other communities who have generally reported a rise in macrosomia rate.[2,3] The decrease in the Maltese population may in fact be an apparent rather than a real one resulting from the definition of macrosomia used. In the absence of specific centile weights by gestation for the Maltese population, macrosomia is generally defined as a birth weight greater than 4000 gm. This definition excludes those infants weighing less than 4000 gm, but who are macrosomic for their gestational age. The socio-biological changes that have been observed in the Maltese population during the period have included an increasing predisposition towards having pregnancies either before 20 years or after 40 years of age, and were more likely to be primiparous.[6] The present study has shown that macrosomic infants were more likely in elderly women aged more than 30 years and in multipara patients with a history of at least one previous pregnancy or miscarriage. These observations suggest that while a definite relationship exists between maternal biological factors and the development of fetal macrosomia, changing patterns were probably not the cause for the temporal decrease noted in the incidence of macrosomia in the Maltese population. A more likely cause for the observed decrease is the increasing predisposition to obstetric intervention with earlier delivery of infants who may still be macrosomic for their gestational age but weighing less than 4000 gm.

Maternal conditions that have a definite relationship to fetal growth promotion include maternal obesity and diabetes. These two factors have been repeatedly shown to be causative factors for fetal macrosomia.[1,2,8] The present study confirms these relationships. The role of hyperglycaemia in the development of macrosomia has long been established. Fetal growth is a multifactorial complex phenomenon with an intricate interaction and overlap of different contributing mechanisms. These mechanisms are the result of the genetic drive to growth, environmental factors and the supply of substrates to the fetus. In addition there is the influence of fetal hormone-dependent growth such as insulin and insulin-like growth factors.[9] The classic relationship between the maternal hyperglycaemia causing fetal hyperinsulinism causing macrosomia has long been accepted,[10] though this has been tempered by contributions of other maternal fuels. It is more difficult to relate macrosomia with obesity especially in the presence of a normal glucose tolerance test and euglycaemia.[11,12] The fetus of the euglycaemic obese woman can be presumed to have been exposed to normal mean glucose values and thus produced normal levels of fetal insulin and insulin-like growth factors. The observed macrosomia in fetuses born to obese women with normal glucose tolerance suggests that the mechanisms promoting excessive fetal growth are more complex than the classic fetal hyperinsulinaemia causation. The relationship of obesity with macrosomia may reflect an inherent insulin-resistance syndrome that at the time of glucose tolerance testing shows metabolic compensation. The relationship between placental receptors to maternal insulin and growth of the infant has still to be fully elucidated. Macrosomia has been shown to be a predictor of the eventual development of metabolic syndrome in the Maltese mothers eight years after delivery.[13] The possible sub-clinical insulin-resistance syndrome in these obese women delivering macrosomic infants may account for the higher predisposition of previous miscarriages noted in the present study since insulin-resistance syndrome has been previously associated with recurrent miscarriages.[14] The inverse relationship between macrosomia and hypertension can be explained by the predisposition of placental insufficiency generally associated with hypertensive disease.

Infant size has repeatedly been shown to influence the obstetric outcome.[1,8,15,16] The present study confirms the previous observations showing an increased predisposition for Cesarean delivery or operative vaginal interventions and shoulder dystocia. The infant outcome was not significantly adversely affected by macrosomia, possibly because of the high Cesarean section rate resorted to in the management of these cases. Macrosomia has also been, in the Maltese population, associated with long-term morbidity in the predisposition for the metabolic syndrome related to adult-onset insulin resistance.[17] This predisposition may be further

augmented by the greater predisposition of very large macrosomic infants >4500 gm to being artificially fed.

Macrosomia reflects the presence of maternal conditions that directly or indirectly influence fetal growth. The association between macrosomia and diabetes has been related to chronic fetal hyperinsulinism, but such an association has not been clearly demonstrated in euglycaemic obese women. Further investigations need to be undertaken to relate macrosomia to the presence of insulin-resistance metabolic syndrome or polycystic ovarian disease. The understanding of the true pathophysiology for the development of macrosomia would enable correct effective intervention therapies to be identified and introduced in clinical practice. While a decrease in macrosomia rate would contribute towards decreasing the maternal and fetal morbidity, an even more important benefit may be the beneficial influence on the long-term consequences of macrosomia.

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