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Neonatal outcome of macrosomic infants: an analysis of a two-year period

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ABSTRACT

Objective: To assess the neonatal outcome of macrosomic neonates in uncomplicated, singleton, term deliveries.
Study design: A retrospective analysis was performed on 5738 live-born term neonates born in the period 2008–2009. The neonatal outcomes were compared between two birth weight (BW) groups: the macrosomic neonates born with BW ≥ 4000 g and a control group: 2500–3999 g. There were 410 (7.1%) neonates in the macrosomic group, 4757 (82.9%) in the control group, while 571 (10.0%) were less than 2500 g at birth. A correlation analysis of two subgroups of the macrosomic neonates (4000–4499 g vs. ≥4500 g) was also carried out.
Results: The rate of caesarean section (CS) was significantly higher in the macrosomic group as compared with the control group (49.3% vs. 39.9%), as were the prevalences of hypoglycaemia (6.1% vs. 2.9%), adrenal haemorrhage (0.98% vs. 0.15%) and the male to female ratio (2.15 vs. 0.95). The rate of icterus was significantly higher in the control group (30.4% vs. 18.5%). The macrosomic subgroups were similar in many aspects, but we found significantly more neonates in the higher weight subgroup as regards a low Apgar score, clavicle fracture and the need for intensive care.
Conclusions: The macrosomic infants were born in good general condition, although those with BW ≥4500 g more frequently had an adverse outcome. The macrosomic and control groups' data revealed significant differences in the rate of CS, the male to female ratio, hypoglycaemia and adrenal haemorrhage.

1. Introduction

There is no general consensus about the definition of the term fetal macrosomia. It can be utilized for neonates with a birth weight (BW) greater than 4000, 4500 or 5000 g, irrespective of the gestational age (GA) as an absolute limit [1]. However, the American College of Obstetricians and Gynaecologists suggests a threshold of 4500 g, as the morbidity increases sharply beyond this [2]. The prevalence of macrosomia has been increasing in recent decades, with an accompanying elevated risk of an adverse outcome for mother, fetus and neonate. It is well known that there are differences in neonatal anthropometric data across geographical populations; for instance, the incidence of macrosomia varies between 5% and 20% [3].

The cause of fetal macrosomia still cannot be determined exactly, since it seems to involve several factors, including environmental, genetic, maternal and fetal features [4–6]. Among the factors which influence fetal macrosomia are primarily the genes which regulate hormones, such as insulin, insulin-like growth factors and their receptors, and other hormones such as thyroxin and leptin. With the upcoming concept of epigenetic regulation, it has become evident that nutritional and other environmental factors during fetal life may modify the long-term expression of genes. Pedersen [7,8] hypothesized that maternal hyperglycaemia stimulates fetal hyperinsulinaemia, which mediates growth. The risk factors also include maternal diabetes mellitus (both pre-gestational and gestational), impaired glucose tolerance, prolonged gestation (>41 weeks), maternal obesity, a pregnancy weight gain >20 kg, maternal height, multiparity, male fetal sex, white maternal race and a previous large infant [9–11]. Modifiable hazard factors include lifestyle related issues of the mother: an increased maternal nutritional intake, a low level of physical activity. Smoking reduces BW, but in general, the non-smoking mothers have healthier neonates compared to smoking mothers [12]. Fetal diseases, such as erythroblastosis fetalis, nesidioblastosis, tumours and numerous syndromes [13] can result in heavy babies.

Fetal overgrowth has both short- and long-term perspectives for the fetus and for the mother. The short-term maternal risks

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include prolonged labour, perineal lacerations, uterine atonia, abnormal haemorrhage and CS [14]. Besides, the fetus has higher risk of shoulder dystocia [15], hypoxia, plexus injuries [16], hypoglycaemia, congenital anomalies and need for intensive care [17,18]. Among the long-term risks type 2 diabetes, cardiovascular disease, obesity [19,20] and childhood cancers have to be mentioned [21,22].

Our present aim is first of all to compare the adverse neonatal outcome in macrosomic and control groups. Secondly, we analyse the macrosomic subgroups in details in order to explore a possible correlation between morbidities and BW. Finally, we plan to investigate the role of diabetes in the morbidity of the macrosomic subgroups.

2. Materials and methods

This is a retrospective study on singleton pregnancies of women who delivered between 01.01.2008 and 31.12.2009 at the Department of Obstetrics and Gynaecology, University of Szeged, Hungary. The inclusion criteria were a GA at delivery of at least 37 completed weeks and a BW of at least 2500 g. There were two main groups: the first group comprised neonates with BW 2500–3999 g; this was the control group. The second group comprised the neonates weighing at least 4000 g. These neonates were further stratified into two subgroups concerning their weights (4000–4499 g, and ≥4500 g) and concerning the diabetic history of the mother.

The neonatal outcome was investigated: the umbilical cord blood pH, the 5-min Apgar score, fracture of the clavicle, cephalhaematoma, adrenal haemorrhage, neurological disorders, congenital anomalies, hypoglycaemia, hyperbilirubinaemia, respiratory disorders, need for intensive care, mechanical ventilation and perinatal mortality.

The definition of hypoglycaemia was a blood glucose level <2.6 mmol/l. Blood glucose was checked at 1, 3, 6, 24 and 72 h of age, or more frequently in the event of hypoglycaemia.

Screening for gestational diabetes mellitus (GDM) was performed by the WHO recommended use of 75-g oral glucose tolerance test (OGTT) at gestational weeks of 24–28. The diagnosis of GDM is made when the fasting and 2-h glucose values are sufficient for a diagnosis of either impaired glucose tolerance or diabetes. Those pregnant with risk factors for GDM underwent the screening in early pregnancy, and in case of negative OGTT a repeated test was done at 24–28 gestational weeks. Hyperbilirubinaemia was defined according to the Clinical Practice Guideline of the American Academy of Pediatrics published in 2004 [23]. Adrenal haemorrhage was diagnosed by ultrasound, as part of the existing routine abdominal ultrasound screening program at the Department of Obstetrics and Gynaecology, University of Szeged.

Statistical analysis was performed by using Chi-Square test; a level $p < 0.05$ was considered to be statistically significant.

3. Results

A total of 5738 singleton births were included in the study from the 2-year period; 410 of the newborns were macrosomic, an incidence of 7.1%. The heaviest baby weighed 5500 g; he was born to a non-diabetic mother.

Among the mothers of the 410 macrosomic infants, 43 (10.5%) had diabetes: 9 (2.2%) were pre-gestational and 34 (8.3%) gestational diabetes. In the control group, 316 (6.6%) mothers had diabetes: 26 (0.5%) were pre-gestational and 290 (6.1%) gestational diabetes. The prevalence of maternal diabetes was significantly higher in macrosomic group than in the control group (10.5% vs. 6.6%; $p < 0.05$).

Table 1
Outcome measures of control group and macrosomic neonates.

	Control	Macrosomic	p
Total	4757	410	
Caesarean section	1898 (39.9%)	202 (49.3%)	<0.001*
Males	2322 (48.8%)	280 (68.3%)	<0.001*
Umbilical cord pH < 7.2	705 (14.8%)	70 (17.0%)	0.22
Apgar score < 7 at 5 min	87 (1.8%)	4 (0.9%)	0.22
Congenital anomalies	185 (3.8%)	18 (4.3%)	0.68
Hypoglycaemia	138 (2.9%)	25 (6.1%)	<0.001*
Polycythaemia	161 (3.4%)	19 (4.6%)	0.19
Hyperbilirubinaemia	1446 (30.4%)	76 (18.5%)	<0.001*
Clavicle fracture	43 (0.9%)	7 (1.7%)	0.11
Cephalhaematoma	135 (2.8%)	15 (3.6%)	0.34
Adrenal haemorrhage	7 (0.15%)	4 (0.98%)	<0.001*
Respiratory disorder	305 (6.4%)	21 (5.1%)	0.26
NICU admission	210 (4.4%)	21 (5.1%)	0.58

* Significance at $p < 0.05$.

Table 1 summarizes the statistical data and an analysis of the control and macrosomic groups.

The number of caesarean sections in the macrosomic group was 202 (49.3%), which was significantly more frequent ($p < 0.001$) than in the control group: 1898 (39.9%). It was a very interesting finding that the male–female ratio among the macrosomic infants was 2.15 to 1, whereas in the control group it was 0.95 to 1. The difference was significant ($p < 0.001$). As concerns the general condition of the macrosomic infants at birth, in 70 (17.0%) neonates the umbilical cord pH was <7.2, but most of them showed a quick recovery. Fortunately, only 4 (0.9%) of the 70 neonates had a 5-min Apgar score < 7. Intensive care unit (NICU) admission was needed for 21 (5.1%) patients either at secondary or tertiary care, 21 (5.1%) had a respiratory disorder. Hypoglycaemia was found in 25 (6.1%) cases among the macrosomic infants, and 138 (2.9%) in the control group; the difference was significant ($p < 0.001$). The incidence of polycythaemia did not differ significantly. As concerns the incidence of birth trauma, there was no significant difference in clavicle fracture, cephalhaematoma. There was a highly significant difference in the incidence of adrenal haemorrhage: 4 (0.98%) vs. 7 (0.15%); $p < 0.001$. The only parameter which was significantly higher in the control group was the rate of hyperbilirubinaemia 1446 (30.4%) vs. 76 (18.5%); $p < 0.001$. In both study groups, the perinatal mortality was zero.

The statistical comparison of congenital anomalies regarding their relation to the weight and diabetic history of mother are detailed in Table 2, without significant difference.

Statistical correlation analysis of the 4000–4499 g and ≥4500 g subgroups (Table 3) revealed significantly more cases in the higher weight group as regards an Apgar score < 7 at 5 min, clavicle fracture, and NICU admission. In the case of polycythaemia, the correlation was very close to being significant.

Table 2A
Congenital malformations in the control and macrosomic groups.

	Control n = 4767	Macrosomic n = 410	p
Congenital malformations	185 (3.9%)	18 (4.4%)	0.62

Table 2B
Congenital malformations of the macrosomic neonates of diabetic and non-diabetic mothers.

	Diabetic n = 43	Non-diabetic n = 367	p
Congenital malformations	4 (9.3%)	14 (3.8%)	0.1