Risk Factors and Pregnancy Outcomes of Macrosomia: a Retrospective Cohort Study

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Objectives: To evaluate maternal risk factors associated with macrosomia (birthweight ≥4000 g), and perinatal outcomes in Hong Kong.
Methods: This was a retrospective cohort study conducted at a regional obstetric unit over a 5-year period. All singleton pregnancies with livebirths delivered at term (≥37 weeks of gestation) were analysed. Maternal epidemiological and anthropometric characteristics, presence of antenatal complications (gestational diabetes and medical disorders), and pregnancy outcomes (need for labour induction, mode of delivery, Apgar scores, occurrence of shoulder dystocia, and birth trauma) were compared between macrosomic and non-macrosomic pregnancies. Logistic regression analysis was conducted to identify risk factors associated with macrosomia.
Results: From 2012 to 2016, 19 614 singleton, term livebirths were identified. Of these, 567 (2.89%) babies had a birthweight of ≥4000 g. A logistic regression model confirmed that the most prominent risk factor for macrosomia was post-term pregnancy (adjusted odds ratio [OR]=4.80), followed by diabetic complications in pregnancy (adjusted OR=3.90), maternal obesity (adjusted OR=1.65), multiparity (adjusted OR=1.50), and previous miscarriages (adjusted OR=1.35). Women with macrosomic pregnancy were more likely to be delivered by Caesarean section (36.0% vs. 20.8%), have failed instrumental deliveries (11.10% vs. 4.18%), have wound complications (1.23% vs. 0.23%), and experience postpartum haemorrhage (16.60% vs. 6.48%). Macrosomic neonates were more likely to encounter shoulder dystocia (5.23% vs. 0.40%) and birth trauma (0.50% vs. 0.05%).
Conclusion: The incidence of macrosomic pregnancy in this local population (2.89%) was significantly lower than that reported in western populations. Our data confirm an increased likelihood of maternal and neonatal morbidities in these pregnancies.

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Introduction

Macrosomia is associated with excess risks of adverse pregnancy outcomes and is a challenge in obstetrics[1]. The definitions of macrosomia vary from a birthweight of ≥4000 g to ≥4500 g and ≥5000 g[2]. In many western countries, the rate of macrosomic births has increased since the 1990s[3,4]. Reports worldwide have in general documented an increase in mean birthweight, mean birthweight for gestational age, and the prevalence of large for gestational age in recent decades[5]. A study in Beijing reported an increase in overall birthweight over a 15-year period from 1996 to 2010[6]. Another study in China showed an increase in the prevalence of macrosomia from 6% in 1994 to 7.3% in 2014[7]. Macrosomia is associated with many adverse maternal and neonatal outcomes. For mothers, macrosomia has been associated with increased risks of Caesarean section, prolonged labour, postpartum haemorrhage, and third- and fourth-degree perineal lacerations. Macrosomic neonates are more prone to birth trauma, perinatal asphyxia, shoulder dystocia, and perinatal death[8]. In a Hong Kong study, increasing birthweight was strongly linked to the risk of shoulder dystocia[9]. In addition, children who are born macrosomic and exposed to an intrauterine environment of maternal obesity or diabetes are at increased risk of developing metabolic syndrome later in life[10].

We reviewed the incidence of macrosomia among singleton, term livebirths in a Hong Kong population and attempted to evaluate the risk factors of macrosomia. We also reviewed the pregnancy outcomes of macrosomia to determine whether the incidence of adverse perinatal outcomes was in line with that reported in the literature.

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Methods

This study was approved by the ethics committee of the Kowloon Central Cluster of the Hospital Authority. All singleton pregnancies with a livebirth delivered at term (≥37 weeks of gestation) over a 5-year period from 2012 to 2016 at the United Christian Hospital were analysed. Data were extracted from the electronic obstetrics clinical information system database and the antenatal record system. Additional clinical details were extracted from the labour ward registry, individual clinical notes of the women, and the paediatric clinical records of the neonates. Macrosomia was defined as a birthweight of ≥4000g. The gestation at delivery was defined as the number of completed weeks of gestation, according to either the number of weeks of amenorrhea or confirmation by ultrasonography. Special care baby unit admission was defined as admission of the neonate immediately and up to 28 days after birth. Maternal obesity was defined as a body mass index (BMI) of ≥25 kg/m^2 before pregnancy or in the first trimester of pregnancy. The diagnosis of gestational diabetes and diabetes in pregnancy was based on the 75-g oral glucose tolerance test, according to the World Health Organization 2013 criteria and in accordance with our departmental protocol. Birth trauma included cranial haemorrhage (subgaleal and subdural), clavicle and other long bone fractures, and brachial plexus injury.

Maternal epidemiological and anthropometric characteristics, presence of antenatal complications (gestational diabetes and medical disorders), and pregnancy outcomes (maternal need for labour induction, mode of delivery, Apgar scores, occurrence of shoulder dystocia, and birth trauma) were compared between macrosomic and non-macrosomic pregnancies. Continuous variables were compared with Student's *t* test, and categorical variables with the Chi-square test or Fisher's exact test, as appropriate. A logistic regression model was constructed using significant variables on univariate analysis to identify risk factors associated with macrosomia, with adjusted odds ratios (ORs) and 95% confidence intervals (CIs) reported. A p value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS (Windows version 23; IBM Corp, Armonk [NY], US).

Table 1. Incidence of macrosomic pregnancy per year

Year	Frequency	Percentage
2012	144/4908	2.93
2013	107/3797	2.81
2014	114/4020	2.83
2015	107/3931	2.62
2016	95/3286	2.42

Results

Of the 19614 singleton term livebirths identified from 2012 to 2016, 567 (2.89%) were considered to be macrosomia (birthweight ≥4000 g). Over the 5 years, the annual incidence of macrosomia ranged from 2.42% to 2.93% (p=0.98, Table 1).

Univariate analysis showed that women with macrosomic pregnancies were significantly older than others (32.9 vs. 31.9 years, p<0.001), with a higher proportion having advanced maternal age (39.5% vs. 31.1%, OR=1.44, p<0.001), being multiparous (62.1% vs. 51.5%, OR=1.54, p<0.001), and having had previous miscarriages (56.4% vs. 45.0%, OR=1.58, p<0.001). In addition, a higher proportion of these women had previous Caesarean deliveries (21.5% vs. 17.9%, OR=1.25, p=0.03) probably related to the fact that more were multiparous. They also had a higher BMI in early pregnancy (24.4 vs. 23.3 kg/m^2, p<0.001) and a higher incidence of obesity with BMI of ≥25 kg/m^2 (38.6% vs. 26.0%, OR=1.78, p<0.001). Women with macrosomic pregnancies had a higher incidence of post-term delivery beyond 41 weeks (28.7% vs. 10.5%, OR=3.42, p<0.001), and a longer gestation at delivery (39.8 vs. 39.1 weeks, p<0.001). There was also a higher incidence of gestational diabetes or diabetes in pregnancy among macrosomic pregnancies (28.7% vs. 11.6%, OR=3.06, p<0.001), but the incidence of pre-eclampsia or other antenatal medical complications did not differ significantly between groups (Table 2).

A logistic regression model was constructed with macrosomia as the dependent variable and significant factors on univariate analysis as independent variables. The most prominent risk factor for macrosomia was post-term pregnancy (adjusted OR=4.80, 95% CI=3.93-5.87, p<0.001), followed by diabetic complications in pregnancy (adjusted OR=3.90, 95% Cl=2.92-4.40, p<0.001), maternal obesity (adjusted OR=1.65, 95% CI=1.38-1.97, p<0.001), multiparity (adjusted OR=1.50, 95% CI=1.23-1.83, p<0.001), and previous miscarriages (adjusted OR=1.35, 95% CI=1.12-1.60, p=0.001). Advanced maternal age and previous Caesarean section were excluded from the equation (Table 3).

Women with macrosomic pregnancy were more likely to have induced labour (30.5% vs. 15.4%, OR=2.4,

Table 2. Maternal characteristics in macrosomic and non-macrosomic pregnancies

Variable	Macrosomia (n=567)*	Non-macrosomia (n=19047)*	Mean difference (95% confidence interval)	Odds ratio (95% confidence interval)	p Value
Maternal age (years)	32.9 ± 5.03	31.9 ± 5.13	1.01 (0.59-1.44)	-	<0.001
Advanced age (≥35 years)	224 (39.5)	5927 (31.1)	-	1.44 (1.21-1.71)	<0.001
Parity			-	1.54 (1.23-1.83)	<0.001
Nulliparous	215 (37.9)	9235 (48.5)			
Multiparous	352 (62.1)	9812 (51.5)			
Previous miscarriages	320 (56.4)	8571 (45.0)	-	1.58 (1.33-1.87)	<0.001
Previous Caesarean section	122 (21.5)	3417 (17.9)	-	1.25 (1.02-1.53)	0.03
Maternal height (cm)	158.3 ± 4.97	156.4 ± 5.41	1.87 (1.41-2.32)	-	<0.001
Early pregnancy weight (kg)	61.1 ± 7.95	56.9 ± 8.41	1.87 (1.42-2.32)	-	<0.001
Body mass index (kg/m^2)	24.4 ± 3.02	23.3 ± 3.22	1.14 (0.88-1.42)	-	<0.001
Maternal obesity (body mass index of ≥25 kg/m^2)	219 (38.6)	4963 (26.0)	-	1.78 (1.50-2.12)	<0.001
Gestation at delivery (weeks)	39.8 ± 1.06	39.1 ± 1.11	0.73 (0.64-0.82)	-	<0.001
Post-term pregnancy (≥41 weeks)	163 (28.7)	2009 (10.5)	-	3.42 (2.83-4.12)	<0.001
Gestational diabetes / diabetes in pregnancy	163 (28.7)	2213 (11.6)	-	3.06 (2.54-3.70)	<0.001
Pre-eclampsia	9 (1.58)	327 (1.71)	-	0.92 (0.47-1.80)	1.0
Other medical disorders†	20 (3.53)	479 (2.51)	-	1.41 (0.89-2.23)	0.13

* Data are presented as mean ± standard deviation or No. (%) of subjects

† Including significant medical (cardiac, thyroid, neurological, autoimmune, renal) diseases in pregnancy requiring treatment

Table 3. Logistic regression analysis of risk factors for macrosomia

Variable	B	Standard error	Wald	Adjusted odds ratio (95% confidence interval)	p Value
Variables in the equation					
Post-term pregnancy	1.57	0.102	234	4.80 (3.93-5.87)	<0.001
Gestational diabetes	1.27	0.105	149	3.90 (2.92-4.40)	<0.001
Maternal obesity	0.50	0.089	31.6	1.65 (1.38-1.97)	<0.001
Multiparity	0.40	0.10	16.1	1.50 (1.23-1.83)	<0.001
Previous miscarriages	0.29	0.09	10.7	1.35 (1.12-1.60)	0.001
Variables not in the equation					
Advanced maternal age	0.07	0.094	0.61	1.08 (0.89-1.29)	0.43
Previous Caesarean section	-0.005	-0.12	0.002	0.99 (0.79-1.25)	0.96

p<0.001). They were more likely to be delivered by Caesarean section (36.0% vs. 20.8%, OR=2.12, p<0.001) rather than normal vaginal delivery (57.0% vs. 69.8%) or instrumental delivery (7.0% vs. 9.4%). Moreover, the risk of failed instrumental delivery was higher for macrosomic pregnancies (11.10% vs. 4.18%, OR=2.85, p=0.024) and the risk of shoulder dystocia was also higher (5.23% vs. 0.40%, OR=10.90, p<0.001). The average blood loss at delivery in macrosomic pregnancies was significantly higher (333 vs. 225 ml, p<0.001), and the incidence of postpartum haemorrhage was also higher (16.60% vs. 6.48%, OR=2.86, p<0.001). After delivery, those with macrosomic pregnancies were more likely to have abdominal or episiotomy wound complications, including significant wound infection and gaping wound requiring re-suturing (1.23% vs. 0.23%, OR=5.39, p=0.001) [Table 4].

Table 4. Maternal and neonatal outcomes in macrosomic and non-macrosomic pregnancies

Variable	Macrosomia (n=567)*	Non-macrosomia (n=19047)*	Mean difference (95% confidence interval)	Odds ratio (95% confidence interval)	p Value
Induction of labour	173 (30.5)	2942 (15.4)	-	2.40 (2.00-2.88)	<0.001
Mode of delivery			-	2.12 (1.78-2.53)†	<0.001
Normal vaginal	323 (57.0)	13285 (69.8)			
Instrumental	40 (7.0)	1785 (9.4)			
Caesarean section	204 (36.0)	3977 (20.8)			
Episiotomy	233/363 (64.25)	9423/15070 (62.50)	-	1.07 (0.86-1.33)	0.51
Failed instrumental delivery	5/45 (11.10)	78/1863 (4.18)	-	2.85 (1.09-7.44)	0.024
Wound complications (severe wound infection and gaping wound requiring re-suturing)	7 (1.23)	44 (0.23)	-	5.39 (2.42-12.00)	0.001
Blood loss at delivery (ml)	333 ± 287	225 ± 247	108 (88-129)	-	<0.001
Postpartum haemorrhage	94 (16.60)	1235 (6.48)	-	2.86 (2.28-3.60)	<0.001
Postnatal deep venous thrombosis	2 (0.35)	18 (0.09)	-	3.74 (0.86-16.20)	0.057
Birthweight (g)	4204 ± 195	3205 ± 332	998 (970-1025)	-	<0.001
Apgar score of ≤7 at 5 min	3 (0.50)	51 (0.26)	-	1.98 (0.61-6.36)	0.20
Shoulder dystocia	19 (5.23)	60 (0.40)	-	10.90 (6.50-18.50)	<0.001
Birth trauma	3 (0.50)	10 (0.05)	-	10.10 (2.78-36.90)	0.006
Cranial haemorrhage	1	2			
Brachial plexus palsy	2	1			
Fractures	0	6			
Special care baby unit admission	559 (98.6)	7304 (38.3)	-	112 (55-225)	<0.001
Neonatal death	0	1 (0.005)	-	11 (0.45-274)	1.0

* Data are presented as mean ± standard deviation or No. (%) of subjects

† Caesarean section versus vaginal delivery

Macrosomic babies were of higher birthweight (4204 vs. 3205 g, p<0.001) and were more prone to have birth trauma (0.50% vs. 0.05%, OR=10.10, p=0.006). Their rate of special care baby unit admission was also higher (98.6% vs. 38.3%, OR=112, p<0.001). There was no significant difference in the rate of low Apgar scores or neonatal death between groups (Table 4).

Discussion

Our data confirm that post-term pregnancy, diabetic complications in pregnancy, and maternal obesity are the main risk factors associated with macrosomia. In our cohort, the overall incidence of macrosomia was 2.89%, which is lower than that in other studies in Chinese populations, of 7.3% to 8.7%[6,7]. The incidence of macrosomia in our cohort was also much lower than that reported in other populations. The incidence of macrosomia (birthweight >4 kg) was 7.1% in a large French cohort of 27 000 women and 9.5% in a Canadian cohort of 22 000 women[11]. Similarly, the incidence was 7.47% in a Turkish study, despite a gestational diabetes rate of only 4.8%[12].

There seem to be wide variations in the incidence of maternal obesity in different populations. Using the Asian BMI cut-off of 25 kg/m^2 in our cohort, the overall incidence of maternal obesity was 26.4%, whereas the incidence of women with pre-pregnant BMI of ≥24 kg/m^2 was only 13% to 16% in a Beijing survey[7]. Maternal obesity is more prevalent in western populations. The incidence of overweight (BMI 25-30 kg/m^2) and obesity (BMI >30 kg/m^2) was 18.6% and 9.1% in a French cohort and 23.5% and 16% in a Canadian cohort, respectively[11]. In a large cross-sectional survey of 268 000 deliveries from 2011 to 2014 in Wisconsin, United States, the incidence of maternal obesity (BMI >30 kg/m^2) was 27.8%[13]. In another North American study, the incidence of overweight and

obesity was 26.5% and 23.3%, respectively[14]. Although the incidence of obesity was quite high in this local cohort, maternal obesity seems to be a greater problem for concern for many western populations.

In our cohort, the most prominent risk factor for macrosomia was post-term pregnancy, with an adjusted OR of 4.80. Women with macrosomic pregnancy were more likely to have induced labour. This finding could be attributed to an increased induction rate for post-term pregnancy and for gestational diabetic complications. According to our hospital's protocol, post-term pregnancies with gestational age of ≥41 weeks are routinely offered induction of labour. Those who have gestational diabetes are offered induction of labour at ≥40 weeks if they are treated by diet control. If the diagnosis is diabetes in pregnancy or if the gestational diabetes requires insulin for control, induction of labour is offered even earlier, at ≥38 weeks, in line with the recommendations from the National Institute for Health and Care Excellence guidelines[15]. Many experts advocate induction of labour before 41 weeks when the estimated fetal weight is up to >2 standard deviations on ultrasonography. Our protocol does not specifically include suspected macrosomia as an indication for induction of labour. This practice remains controversial. In a retrospective series, an analysis of pregnancies in which neonates had a birthweight of 4 kg showed that induction of labour at 39 weeks' gestation was associated with a lower rate of Caesarean section when compared with deliveries at 40 to 42 weeks[16]. In a large multicentre trial in Europe in which women with a singleton fetus whose estimated weight exceeded the 95th centile were randomly assigned to either induction of labour between 37 and 39 weeks or expectant management, induction of labour was associated with a reduced risk of shoulder dystocia and morbidities and higher likelihood of spontaneous vaginal delivery[17]. In contrast, the 2016 updated Cochrane review[18] included four trials involving 1190 women and concluded that compared with expectant management, induction of labour for suspected macrosomia did not reduce the risk of Caesarean section or instrumental delivery. Although shoulder dystocia and any fractures were reduced in the induced labour group, perinatal morbidity was not significantly different between groups[18].

The issue of elective abdominal delivery for suspected macrosomia remains even more controversial. Elective Caesarean section has been proposed for suspected macrosomia of ≥5000 g in uncomplicated pregnancies and ≥4500 g if maternal risk factors such as diabetes or shoulder dystocia in previous pregnancies are identified[19]. Nonetheless, the estimation of fetal weight at such high ranges has been shown to be less accurate than when fetal weight is within the normal range[20], and specific formulae are needed to improve precision. In addition, any error could be due to the time lapse between ultrasonography and delivery[21]. A retrospective review reported that ultrasonography could detect only 33% of macrosomic fetuses, so a policy of elective Caesarean section for macrosomia would likely miss a large proportion of target pregnancies[22]. In addition, it was estimated that the number-needed-to-treat by Caesarean section would be 10.6 to avoid one shoulder dystocia, 52.6 to avoid one plexus injury, and 23.5 to avoid one sphincter laceration[1]. Thus, the role of elective Caesarean section may be appropriate only for extreme macrosomia.

Previous miscarriage is another risk factor for macrosomia and has been reported in other studies as higher gravida[2]. Women with macrosomic pregnancy are more likely to be multiparous and have had more pregnancies. They are more likely to be of advanced maternal age and obese; both factors are associated with an increased risk of miscarriage.

In general, women with macrosomic pregnancy experience a more difficult delivery and more adverse outcomes and have higher rates of failed instrumental delivery, birth trauma, and shoulder dystocia[23], as well as a higher rate of postpartum haemorrhage during delivery[24]. In a large Chinese cohort, neonates with a birthweight of >4.5 kg had higher rates of infant mortality, an Apgar score of ≤3 at 5 minutes, and respiratory and neurological disorders[23]. Nonetheless, our data showed no significant difference in Apgar scores between macrosomic and non-macrosomic neonates. This finding was probably related to the comparatively smaller size of our cohort, with only a very small proportion of neonates with a birthweight of ≥4.5 kg (n=43, 0.22%).

This study had several limitations. It was retrospective and the mode of delivery was often dictated by clinical suspicion of macrosomia. Ultrasonography for fetal weight estimation was performed selectively in indicated cases. In addition, we were unable to analyse total weight gain in pregnancy, as these data were heterogeneous owing to the incomplete recording of pre-pregnancy weight. The high rate of special care baby unit admission could be attributed to the routine admission of neonates with a birthweight of ≥4 kg, according to the paediatrician's protocol and may not reflect actual perinatal morbidity.

Conclusion

Our data confirm that macrosomic pregnancies are associated with higher maternal and neonatal morbidity as compared with non-macrosomic pregnancies. The main predictive factors associated with macrosomia were post-date pregnancies, gestational diabetes, maternal obesity, and multiparity. Further studies should focus on the role of induced labour at term for suspected macrosomia, more stringent control of gestational diabetes during pregnancy, and the reduction of maternal obesity in the general obstetric population.

Declaration

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