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# Yvonne Kwun-Yue Cheng Terence T Lao

Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong **Abstract:** The prediction and management of fetal macrosomia remains an obstetric challenge. Significant maternal and neonatal complications can result from the birth of a macrosomic infant, and include prolonged labor, operative delivery, postpartum hemorrhage, perineal trauma, shoulder dystocia, birth trauma, chorioamnionitis, meconium aspiration, perinatal asphyxia, low Apgar scores, neonatal hypoglycemia, and perinatal mortality. This review article discusses these maternal and perinatal risks and the management of suspected macrosomia.

**Keywords:** macrosomia, large for gestational age, shoulder dystocia, birth trauma, perineal tear

## Introduction

Management of fetal macrosomia has long been an obstetric challenge, and is becoming an increasingly important problem because of its rising incidence and the associated risks to the mother and infant.

Fetal macrosomia has been defined in many different ways, including birth weight of more than 3,600 g, 3,800 g, 4,000 g, or 4,500 g, or more than the 90th percentile for gestational age. By far, 4,000 g is the commonest birth weight cutoff used to define macrosomia. Using this criterion, the incidence in Europe and North America has been reported to be 10%–20%. Recent evidence suggests that the incidence of macrosomia is increasing. A study from Denmark indicated an increase in the frequency of macrosomia from 16.7% in 1990 to 20.0% in 1999. The figures from North America show that the proportion of neonates with a birth weight over the 90th percentile increased by 5%–9% in the USA and reached 24% in Canada between 1985 and 1988. Such a trend was attributed to the increase in maternal anthropometry, reduced cigarette smoking, and changes in sociodemographic factors.

The incidence of macrosomia varies according to ethnicity, and is lower in the Chinese population.<sup>4</sup> Epidemiologic studies have shown that Chinese and South Asian infants are smaller for their gestational age.<sup>5</sup> This difference in birth weight distribution is likely due to the genetic differences and anthropometric discrepancies between populations. From a recent study, the incidence of macrosomia in Chinese population was reported to be only 3.4%.<sup>4</sup>

A number of risk factors associated with macrosomia have been identified, and include maternal body mass index, weight gain, advanced maternal age, multiparity, diabetes, and gestational age >41 weeks.<sup>6</sup> However, it is well known that prediction based on clinical risk factors alone has a very low positive predictive value.<sup>7</sup>

Correspondence: Terence T Lao
Department of Obstetrics and
Gynaecology, The Chinese University of
Hong Kong, Prince of Wales Hospital,
Hong Kong
Tel +852 2632 1290
Fax +852 2636 0008
Email lao-tt@cuhk.edu.hk

Screening for macrosomia by means of maternal factors and first trimester nuchal translucency and biochemical markers (free beta-human chorionic gonadotropin and pregnancy associated plasma protein A) has also been performed, but the detection rate is poor.<sup>8</sup>

Diagnosis and management of macrosomia is a fundamental obstetric problem because it can lead to significant maternal and perinatal morbidity and mortality. These maternal and neonatal complications are reviewed and discussed below.

# **Maternal complications**

# Prolonged labor

The duration of labor is more prolonged for women carrying macrosomic babies, and the risk is increased with increasing birth weight. Both the first and second stages of labor are longer than for normosomic pregnancies, and arrest of descent in the second stage of labor can occur secondary to macrosomia. In a study of macrosomic infants weighing more than 4,500 g, the risk of shoulder dystocia is higher when the second stage is longer than 2 hours, with a crude odds ratio (OR) of 1.17 (95% confidence interval [CI] 0.82–1.66). As expected, primigravidae have a higher incidence of prolonged labor compared with multiparous women when delivering a macrosomic baby weighing more than 4,500 g. Prolonged labor associated with macrosomia is, in turn, a contributor to other maternal complications, including operative delivery and postpartum hemorrhage.

# Operative delivery

The mode of delivery significantly shifts with increasing macrosomia. The incidences of vaginal operative delivery and cesarean section are higher for macrosomic infants. 9,11–13
The overall rate of cesarean section in babies with a birth weight >4,000 g varies widely between different studies and ranges from 14% to 44%. 13–15 The risk of cesarean section escalates with increasing birth weight, and the proportion of vaginal instrumental delivery decreases with increasing birth weight. 9,12 The increased risk of cesarean section is a consistent finding in different countries and in different ethnic groups, and the odds are particularly high for primiparous mothers. 16 In macrosomic births, the risk of shoulder dystocia is associated with the need for vaginal instrumental delivery. 11

# Postpartum hemorrhage

Postpartum hemorrhage occurs more commonly following delivery of macrosomic babies, 9,13,17 and again, the risk

increases with increasing birth weight.<sup>12</sup> This association could be due to a direct consequence of a big baby or as a result of prolonged labor, labor induction, operative vaginal delivery, uterine atony, and perineal tears.

## Perineal trauma

The risk of perineal tears increases 1.5-fold to 2-fold in cases of macrosomia. <sup>18,19</sup> Some investigators suggest that the incidence of major perineal tear rises significantly with greater birth weight, <sup>20</sup> but this has been refuted. <sup>12</sup> The risk appears to be higher in Asian, Filipino, and Indian women than in Caucasian women. <sup>18</sup> Such ethnic differences may be due to differences in body type and discrepancies in perineal anatomy. Major perineal trauma, including third and fourth degree tear, can cause significant long-term anal incontinence, which can have a negative impact on the woman's quality of life.

# Fetal and neonatal complications

Although the literature frequently and consistently demonstrates an increase in perinatal morbidity and mortality with increasing birth weight, the overall incidence of neonatal complications remains low.<sup>21</sup>

# Shoulder dystocia

The incidence of shoulder dystocia ranges between 0.58% and 0.70% in Caucasians.<sup>22</sup> It also appears to vary with ethnicity, with an incidence of only 0.3% in the Chinese population.<sup>4</sup> It has been reported consistently in the literature that the risk of shoulder dystocia escalates with increasing birth weight.<sup>4,6,23,24</sup> However, the incidence of shoulder dystocia in different birth weight groups varies widely between studies. In a recent study in Norway,<sup>24</sup> the incidence was approximately 1%, 2%, 4%, and 6% for birth weights of 4,000-4,199 g, 4,200-4,399 g, 4,400-4,599 g, and  $\ge 4,600$  g, respectively, whereas another study reported an incidence of over 20% when the birth weight was above 4,500 g. Nevertheless, despite such an association, half or even more of the births complicated by shoulder dystocia occur in babies with a birth weight less than 4,000 g.<sup>4</sup>

#### Birth trauma

The incidence of birth trauma, namely brachial plexus and skeletal injuries, increases with rising birth weight. 9,25

#### Brachial plexus injury

Congenital brachial plexus injury (BPI) is defined as flaccid paresis of an upper extremity due to traumatic stretching of

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the brachial plexus at birth, with passive greater than active range of motion. The incidence varies between countries and is approximately 1.5 cases per 1,000 live births. 4.26 Most cases are transient, but permanent damage can occur in 5% of cases, and is often a cause of litigation.

BPI is characteristically related to shoulder dystocia; however, such complications can occur following normal spontaneous vaginal delivery and cesarean section.<sup>27</sup> Both excessive exogenous traction and strong endogenous pushing forces contribute to BPI.<sup>28</sup> The second most important risk factor for BPI is heavy birth weight,23 which is associated with a 14-fold increase in risk.<sup>26</sup> In one study, the prevalence of BPI progressively increased with infant weight, occurring in only 3% of neonates in the 4,500–5,000 g group and 6.7% in the >5,000 g group.<sup>29</sup> Moreover, the risk is further increased when macrosomia and gestational diabetes coexist, with an adjusted OR of 42 (95% CI 4.05–433.64).<sup>23</sup> It has also been reported that BPI among infants weighing ≥4,000 g is more likely to be severe and persistent than in the normosomic group.<sup>30</sup> Because the two main risk factors for congenital BPI, ie, shoulder dystocia and macrosomia, are not easily predictable, it is difficult to foresee and prevent its occurrence.28

#### Skeletal injuries

Similar to BPI, skeletal injuries commonly occur in the presence of shoulder dystocia and are associated with large infants. 11,31 Fracture of the clavicle is five times more common in macrosomic infants, and occurs more often in vaginal delivery than in cesarean section.<sup>21,32</sup> Humeral fractures are less frequent, but also occur in big babies. On the other hand, Gregory et al analyzed neonatal complications following shoulder dystocia and reported that, unlike brachial plexus injury, the risk of having skeletal injuries in macrosomic infants is not higher than in those with normal birth weight.<sup>21</sup> Clavicular fractures are usually managed conservatively and the outcome is most often benign, with complete recovery and no associated neurologic complications. Humeral fractures are managed mainly by closed reduction followed by splinting or traction techniques, and usually do not have long-term sequelae.

#### Chorioamnionitis

Macrosomia is related to chorioamnionitis. The risk of chorioamnionitis slowly and steadily increases as birth weight increases, and the ORs are 1.94, 2.17, and 2.42 for birth weight groups of 4,000–4,499 g, 4,500–4,999 g, and  $\geq$ 5,000 g, respectively.<sup>6</sup>

# Aspiration of meconium

Some studies show that aspiration of meconium is a risk associated with macrosomia. 9,13 Again, the risk increases with rising birth weight. The ORs are 1.28, 1.65, and 2.61 for babies with birth weights of 4,000–4,499 g, 4,500–4,999 g, and >5,000 g, respectively. However, other investigators reported that the association was not statistically significant. 33

## Perinatal asphyxia

The risk of macrosomic neonates suffering from perinatal asphyxia increases 2–4-fold compared with that in normosomic infants. <sup>21,33</sup> The odds of perinatal asphyxia increase considerably with rising birth weight; in one study, the OR was 2.3 if birth weight was 4,500–4,999 g and increased further to 10.5 if birth weight was >5,000 g.<sup>25</sup>

# Poor Apgar scores

Macrosomia has been reported to be associated with poorer Apgar scores. The greater the birth weight, the higher the risk of low Apgar scores. 9,25 Boulet et al showed the OR for a 5-minute Apgar score ≤6 was 1.65 and 3.49 for infants with birth weight 4,500–4,999 g and >5,000 g, respectively, whereas that for a 5-minute Apgar score ≤3 was even higher, with corresponding ORs of 2.01 and 5.20.9 Furthermore, the risk of a low Apgar score is eight times higher in macrosomic babies when the delivery is complicated by shoulder dystocia. In contrast, Weissmann-Brenner et al could not demonstrate any statistically significant difference in low Apgar scores between normal and big babies. 12

# Neonatal hypoglycemia

The risk of neonatal hypoglycemia is higher in heavy babies,  $^{23}$  and the risk increases with increasing birth weight. Neonates with a birth weight >4,500 g had a seven-fold higher risk of having neonatal hypoglycemia, compared with those appropriate for gestation age.  $^{12}$  This risk further increases in the presence of gestational diabetes. Infants with a birth weight  $\ge 4,000$  g delivered by nondiabetic mothers had a 2.4% risk of neonatal hypoglycemia, whereas those whose mothers had gestational diabetes had an incidence of 5.3%.  $^{23}$ 

#### Intrauterine fetal death

Macrosomia has been consistently shown to be associated with a 2–3-fold increase in intrauterine fetal death.<sup>34</sup> Zhang et al showed that birth weights of 4,000–4,499 g were not at increased risk of mortality compared with those born at 3,500–3,999 g; however, those born at 4,500–4,999 g had

a significantly increased risk of stillbirth (OR 2.7, 95% CI 2.2–3.4) and the risk rose dramatically with a birth weight  $\geq$ 5,000 g (OR 13.2, 95% CI 9.8–17.7).<sup>25</sup> Because maternal diabetes is closely related to macrosomia and fetal death, Mondestin et al addressed this complex interaction and showed that the fetal death rate increased in macrosomic fetuses in both diabetic and nondiabetic pregnancies, but the cutoff birth weight was different, being  $\geq$ 4,250 g in nondiabetic women and  $\geq$ 4,000 g in their diabetic counterparts.<sup>35</sup>

# Neonatal and infant mortality

Numerous epidemiologic studies have shown a distinct relationship between birth weight and neonatal and infant mortality, and have consistently demonstrated a reverse J pattern of weight-specific mortality in all populations, where the mortality rates increase at the extremes of birth weight.<sup>36</sup> Compared with a normosomic group of infants with a birth weight of 3,000-3,999 g, babies with a birth weight >5,000 g had a 2-3-fold increase in risk of neonatal death, and a 1.6-2.0-fold increased risk of postneonatal and infant mortality, respectively. Such an association was not identified in babies with a birth weight of 4,000–4,999 g.9 However, a recent study by Zhang et al,25 which included close to 6 million births from the USA, showed that neonates with a birth weight >4,500 g also had a higher early neonatal death rate (OR 1.8), but there was no increase in late or postneonatal death. Early, late, and postneonatal deaths were all significantly increased in those weighing  $\geq 5,000$  g, with ORs of 6.4, 5.2, and 2.3, respectively. The leading cause of early neonatal death in macrosomic babies was asphyxia.

Sudden infant death syndrome is another concern for macrosomic babies, but the current data are conflicting. The majority of postneonatal deaths reported by Zhang et al $^{25}$  were due to sudden infant death syndrome. Infants with a birth weight  $\geq$ 5,000 g have a more than 2-fold increase in risk. However, such a detrimental effect was not identified in other studies, and excessive intrauterine growth (birth weight  $\geq$ 90th percentile) has even been shown to have a protective role in sudden infant death syndrome. $^{37}$ 

# Long-term complications

The Barker hypothesis explains the concept of fetal programming in utero, such that events during early development have a profound impact on the risk for development of future adult disease. Birth weight has been shown to be predictive of a number of adult diseases, such as hypertension, obesity, and insulin resistance.<sup>38</sup> Alterna-

tive explanations for the association between fetal growth and later diseases, mainly genetic factors, have also been proposed.

Increased birth weight has been shown to have a positive association with overweight, insulin resistance, and metabolic syndrome in later life. The risk of developing metabolic syndrome in childhood is highest when there is coexistence of macrosomia and maternal gestational diabetes, and is comparatively less marked in the group with macrosomia alone.<sup>39</sup>

Interestingly, breast cancer has been found to be associated with high birth weight in numerous studies.<sup>40</sup> Those with particularly high birth weight (≥4,500 g) had the most pronounced elevation in risk (OR 3.10, 95% CI 1.18–7.97). It is postulated that this association is mediated in part by hormonal mechanisms that positively influence fetal growth and mammary gland development.

# Prenatal diagnosis of fetal macrosomia

Prenatal estimation of fetal weight is notoriously known to be inaccurate, with errors exceeding 10% of the actual birth weight. 41 In fact, sonographic estimates of birth weight are no better than clinical assessment. The sonographic detection of macrosomic infants >4,000 g is even more unreliable, with a low sensitivity, low positive predictive value. 42 Different formulae for estimated fetal weight have been evaluated and the prediction of macrosomia is poor. The mean detection rates for fetuses with a birth weight of  $\geq 4,000 \text{ g}, \geq 4,300 \text{ g},$ and  $\geq$ 4,500 g were 29%, 24%, and 22%, respectively, and false positive rates were 12% (for ≥4,300 g) and 7% (for ≥4,500 g).<sup>43</sup> Moreover, many researchers have developed additional assessment methods to improve the detection of macrosomia, including two-dimensional and threedimensional assessment of fetal subcutaneous and soft tissue. However, these methods are more time-consuming and technically demanding. Recently, a new formula has been shown to be superior to the traditional formulae for prediction of macrosomia, where 78% of estimates fell within ±5% of the actual weight at birth, 97% within  $\pm 10\%$ , and 100% within ±15% and ±20%.44

# Management of suspected fetal macrosomia

The management of suspected fetal macrosomia continues to be an obstetric challenge. This is due to the inaccuracy of prenatal clinical or sonographic diagnosis as discussed above, and also because of the difficulty in prediction of its complications during labor, in particular, the risk of shoulder dystocia. 4,45

The most effective way to manage macrosomia is probably by prevention. Two of the most important risk factors for macrosomia which can be modifiable are maternal obesity and gestational diabetes. The risk of macrosomia increases with the severity of maternal obesity. Weight loss and also reduction in body mass index between the first and second pregnancies can reduce the risk of large for gestational age births. Achieving optimal glycemic control in diabetic women, especially postprandial glucose control, can also prevent macrosomia and reduce the incidence of shoulder dystocia and birth trauma.

The idea of inducing labor for suspected macrosomia before the baby grows too big, with an aim to reduce operative deliveries and birth trauma, has not been supported by clinical evidence. Induction of labor for suspected macrosomia in nondiabetic women has not been shown to improve either maternal or neonatal outcome. <sup>49</sup> On the other hand, because women with diabetes have a higher risk of shoulder dystocia and birth trauma, <sup>4</sup> the National Institute for Health and Care Excellence guideline currently suggests that pregnant women with diabetes should be offered elective birth by induction of labor after 38 weeks of gestation. <sup>50</sup>

Whether elective cesarean section should be performed to prevent BPI is another controversial issue. It has been estimated that 443 cesarean sections are required to prevent one permanent BPI in diabetic women with an estimated fetal weight >4,500 g, and an exceedingly high number (3,695) of cesarean sections are needed to prevent one permanent BPI in the nondiabetic population.<sup>51</sup> The Royal College of Obstetricians and Gynaecologists and the American College of Obstetricians and Gynaecologists recommend elective cesarean delivery in diabetic and nondiabetic women with estimated fetal weight >4,500 g and >5,000 g, respectively.<sup>22,52</sup> However, these guidelines may not be appropriate for the Asian population because the birth weight cutoff is too high.<sup>4</sup>

#### **Conclusion**

The incidence of macrosomia is likely to increase further in the future because of the increase in maternal age, obesity, and gestational diabetes. Despite the vast amount of research in this area, limitations exist and persist in the prediction and management of macrosomia and shoulder dystocia. Management of suspected macrosomia should be individualized with the aim to minimize maternal and

fetal complications. All maternity staff should be familiar with the unexpected finding of macrosomia at delivery, and respond and manage appropriately. Training has been shown to improve management and neonatal outcomes of births complicated by shoulder dystocia, <sup>53</sup> and regular obstetric drills should be conducted in every maternity unit.

## **Disclosure**

The authors report no conflicts of interest in this work.

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