Management of Large for Gestational Age Fetus

1. Background

The terms used to describe ‘big babies’ are macrosomia and large for gestational age (LGA). Fetal macrosomia is associated with an increased risk of maternal and neonatal complications.1–4 The complications for the mother include a higher risk of an emergency caesarean section (CS), postpartum haemorrhage (PPH) and perineal trauma. For the neonate, complications include an increased risk of shoulder dystocia resulting in brachial plexus injury, fracture of the humerus or clavicle and birth asphyxia.5–11 The prevalence of macrosomia, defined by a cut-off of neonatal birthweight of more than 4000 g, is about 10%.2,11 Despite the association of macrosomia with adverse maternal and neonatal outcomes, and its relatively common occurrence in clinical practice, there is a lack of consensus regarding management of pregnancies with suspected fetal macrosomia. It is recommended, however, that in pregnancies complicated by diabetes and estimated fetal weight (EFW) of more than 4500 g, an elective CS should be offered in order to avoid adverse outcomes. In the case of non-diabetic pregnancies, the guidelines state that where the EFW is more than 5000 g (the prevalence of which is only 0.2%), an elective CS should be considered. However, in the majority of LGA fetuses, EFW between 4000 g and 5000 g, the recommendations are unclear, with conclusions primarily based on limited scientific evidence or expert opinion.12–14

The management options and information provided to women need to be reviewed in light of recent high quality meta-analysis and a systemic review of randomised controlled trials (RCTs).15,16

Thus, a recent RCT15 of 822 pregnancies with LGA fetuses reported that induction of labour (IOL), when compared to expectant management, was associated with a significant reduction in the risk of adverse perinatal outcomes, including shoulder dystocia and fractures. These results were confirmed by four RCTs involving 1190 women which indicated that, compared to expectant management, IOL was associated with a 40% reduction in the risk of shoulder dystocia and an 80% reduction in the risk of fetal fractures.16,17 This evidence favours offering IOL to non-diabetic women with LGA fetuses. Furthermore, the landmark Supreme Court decision on Montgomery versus Lanarkshire Health Board,18 which involved a case of birth asphyxia resulting in cerebral palsy following complications of shoulder dystocia, has significant implications for the provision of information to pregnant women. The ruling emphasises the need to ensure that obstetricians and midwives provide women with standardised information to allow them to make an informed choice, and the need to have accurate up-to-date guidance on the management options.13,19,20

The main objective of this Scientific Impact Paper is to appraise the recent evidence on the prenatal diagnosis and the management of a LGA fetus.

2. Definitions

Macrosomia is a definition based on neonatal birthweight. The commonly used cut-off is 4000 g, although some authors have proposed other cut-offs such as 4500 g or 5000 g.2,4,5

LGA refers to a gestation-dependant definition with cut-offs of 90th, 95th or 97th centiles. A cut-off of 90th centile at 40 weeks of gestation approximates to a neonatal birthweight of 4000 g and is commonly used in clinical practice.21 It is important to appreciate that all macrosomic neonates are LGA, but not all LGA neonates are macrosomic (see Appendix I).
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3. Risk factors for fetal macrosomia

The risk factors for fetal macrosomia include maternal obesity, multiparity, history of a previous pregnancy resulting in a macrosomic neonate, pre-existing and gestational diabetes mellitus (GDM).\(^5,22–24\) A large population-based study\(^5\) of more than 350,000 singleton pregnancies reported that the risk of delivering a macrosomic neonate (more than 4000 g) increased with maternal body mass index (BMI): women who were overweight, with a BMI of 25–30 kg/m\(^2\) had a 1.5-fold increased risk; and those who were obese, with a BMI of more than 30 kg/m\(^2\) had a two-fold increased risk, compared with mothers with a normal BMI. Another study\(^22\) comparing the association of maternal obesity with delivery of macrosomic neonates reported that in mothers with a normal BMI, the risk increased 1.4, 2.4 and 2.9-fold in those who were overweight, obese and morbidly obese, respectively. Parous mothers are more likely to deliver macrosomic neonates, and higher parity is associated with higher risks; those who were grand multiparous had a 1.9-fold higher risk compared with parous mothers in their second to fourth pregnancy, who had a 1.6-fold risk.\(^5\) There is also evidence\(^22,26\) that in women with a previous pregnancy resulting in a macrosomic neonate, the risk of recurrence is significantly increased. In a population-based linkage cohort study\(^25\) of 1793 macrosomic neonates with birthweight of more than 4500 g, a previous pregnancy resulting in a macrosomic neonate increased the risk of subsequent macrosomia by ten times, and that this increased risk remained even after adjusting for confounding factors. Similar results were reported by another study\(^26\) in which the risk for subsequent macrosomia increased by approximately 15-fold with a history of delivering one macrosomic neonate, but increased to 47 times when there was a history of delivering two such neonates in previous pregnancies.

The association between diabetes or abnormal glucose tolerance and fetal macrosomia is consistent. Pre-existing diabetes mellitus is associated with a 1.7–1.8-fold increase in the risk of fetal macrosomia.\(^5,7\) The risk for macrosomia is increased in pregnancies with GDM, as well as in those pregnancies with elevated fasting plasma glucose levels, where the risk is increased two- to three-fold.\(^27\)

4. Consequences of macrosomia

4.1 Obstetric complications

The main obstetric complications associated with macrosomia are increased risks of operative delivery, PPH and perineal injury.\(^6,28–33\) The risk of operative delivery includes increased risk of instrumental delivery as well as emergency CS.\(^5,7\) A large population-based study\(^5\) in North West London examined the risks of intrapartum complications in 293,822 pregnancies that delivered neonates with birthweight between 2500 and 4000 g compared to 36,462 neonates with a birthweight of more than 4000 g. It reported an increased risk of instrumental vaginal delivery and emergency CS (OR 1.76 and 1.84, respectively) in those delivering macrosomic neonates. The study also provided evidence of prolonged first and second stages of labour in pregnancies with macrosomia compared with those without (OR 1.57 and 2.03, respectively). Another study\(^7\) comparing the risk of CS for macrosomic and non-macrosomic fetuses reported that compared with neonates of birthweight 2500–3999 g, where the risk of CS was 13.9%, the risks associated with neonates weighing 4000–4499 g, 4500–4999 g and more than 5000 g were 21%, 33% and 49%, respectively. A multicentre study\(^6\) of 178,709 pregnancies, including 11,372 macrosomic fetuses, found that fetal macrosomia was associated with significantly increased risks of cephalopelvic disproportion (2.6% versus 0.8%) and prolonged first stage of labour (1.8% versus 0.8%). This is unsurprising since a larger head circumference may lead to prolonged first and second stages of labour secondary to cephalopelvic...
disproportion, thus increasing the incidence of failure to progress satisfactorily in labour – factors likely to need either an instrumental vaginal birth or an emergency CS.

The delivery of a macrosomic neonate is also associated with an increased risk of PPH. In a study\(^8\) examining the risk factors of major obstetric haemorrhage, in neonates with a birthweight of more than 4000 g, the odds of a significant maternal blood loss were increased nearly two-fold. Similar results were reported in other studies\(^5-7\) which have shown increased risk of haemorrhage in pregnancies with macrosomic fetuses. This association could be related to uterine atony following prolonged first and second stages of labour, as a result of second stage emergency CS, and due to vaginal and perineal trauma associated with instrumental vaginal deliveries. The vaginal and/or perineal trauma not only leads to immediate complications, such as increased risk of bleeding, but is also associated with long-term risks such as stress incontinence, anal sphincter damage, incontinence and vaginal prolapse.\(^28-33\) There is considerable evidence of a strong association between the neonatal birthweight and the risk of perineal damage, with the delivery of a macrosomic neonate associated with a three- to four-fold increased risk,\(^28,32\) which remains in such pregnancies, even after adjusting for other confounding variables.\(^32,33\) Similarly, pregnancies resulting in macrosomic neonates are associated with a high-risk of injury to the pudendal and perineal nerves, which in turn may lead to urinary stress incontinence and uterovaginal prolapse.\(^29,30\)

### 4.2 Neonatal complications

Neonatal complications are mainly a consequence of shoulder dystocia – primarily brachial plexus injury; direct birth trauma; and birth asphyxia leading to increased risks of perinatal morbidity and mortality.\(^10,11,34,35\) The risk of shoulder dystocia in a low-risk population is relatively low, approximately 1%.\(^11,36,37\) There are several reports suggesting that in pregnancies complicated by macrosomia, this risk can be as high as almost 20 times.\(^10,11\) In a large population-based study\(^11\) of 175 886 pregnancies, the prevalence of shoulder dystocia showed an exponential increase with birthweight: 5.2% in the group with birthweight 4000–4250 g; 9.1% in those with birthweight of 4250–4500 g; 14.3% in those with birthweight of 4500–4750 g; and 21.0% in those with birthweight of 4750–5000 g.

The brachial plexus injuries in macrosomic neonates are secondary to nerve damage due to traction on the fetal head in cases with shoulder dystocia and typically occur in about 1.3–1.5/1000 births.\(^11,38\) Although the majority of cases of brachial plexus injuries occur in neonates weighing less than 4500 g, the risk of brachial plexus injuries is up to 20 times higher in macrosomic neonates compared with those that are non-macrosomic.\(^38-40\) In a qualitative review of 12 studies\(^39\) that reported on the risk of brachial plexus injury following shoulder dystocia, the risk in neonates weighing less than 4000 g, 4000–4499 g and 4500 g or more, were 9%, 18% and 26%, respectively. Moreover, macrosomic neonates were also at an increased risk of fracture of clavicle and humerus. Fracture of the clavicle occurs in 4–6/1000 births, but in macrosomic neonates, this risk is increased ten-fold.\(^41,42\) Although this complication can be seen in non-macrosomic neonates, a retrospective cohort study\(^41\) of 77 543 livebirths including 319 cases of clavicular fracture, reported the risk was significantly higher in macrosomic babies, with 18% of neonates with birthweight of 4000 g or more having a clavicular fracture as opposed to 3.8% of neonates in the control group. A review\(^42\) suggested that although there was considerable heterogeneity in the reported risk factors for clavicular fracture, the single most common risk factor was neonatal birthweight, which remained significant even after controlling for other confounders in a multivariate analysis.

Macroscopic babies are also at an increased risk of complications secondary to perinatal hypoxia, such as low Apgar scores and increased risk of admission to the neonatal intensive care unit.\(^6,43\) The risk of birth asphyxia, and the subsequent long-term neurological sequelae, such as cerebral palsy, neurodevelopmental delay, seizures, cognitive defects, and in some cases perinatal death, may be due
to prolonged first or second stages of labour in pregnancies with LGA fetuses, as well as birth trauma.

In a study\(^{40}\) examining shoulder dystocia-related permanent fetal injury in a group of 316 cases with neurological injury at birth, the incidence of irreversible central nervous system injuries was about 23%. Furthermore, as the EFW increases above 4000 g, the increase in the risk of permanent injury was exponential rather than linear, and was likely to be as high as 10%. This increased risk of long-term irreversible damage remains, even after correcting for other confounding factors.

The evidence regarding association between neonatal macrosomia and risk of hypoglycaemia in non-diabetic pregnancies is unclear. Although there is some evidence to suggest an increased risk,\(^{44,45}\) the lack of evidence to definite causation, led the British Association of Perinatal Medicine\(^{46}\) on identification and management of neonatal hypoglycaemia in full term infants not to recommend routine screening for hypoglycaemia in phenotypically normal neonates born to non-diabetic mothers.

5. Antenatal prediction of large for gestational age neonates

One of the main challenges in establishing a management guideline for pregnancies with suspected fetal macrosomia is the lack of an accurate method of antenatal identification. The National Institute for Health and Care Excellence (NICE) guideline on antenatal care\(^{14}\) states that ultrasound estimation of fetal size for suspected LGA fetuses should not be undertaken in low-risk populations. Similarly, the American Congress of Obstetricians and Gynecologists practice bulletin\(^{47}\) states that the antenatal diagnosis of fetal macrosomia is imprecise and the accuracy of ultrasound biometry is no better than that obtained with clinical palpation.

The common clinical methods for the antenatal diagnosis of macrosomia include measurement of the symphysis fundal height (SFH), abdominal palpation and assessment of EFW using ultrasound biometry. A prospective cohort study\(^{47}\) including 2941 women which examined the accuracy of SFH in predicting neonatal birthweight above the 90th centile reported the detection rate (DR) of macrosomia was modest (38%) with a false-positive rate (FPR) of 12%. Another study\(^{48}\) evaluating the effectiveness of SFH in screening for LGA neonates reported that DRs were quite disappointing for the crude neonatal birthweight and in those adjusted for gestational age – 12% and 20% for EFW more than 4000 and 4500 g, respectively, and 17% and 21% for LGA neonates above the 90th and 97th centiles, respectively. Similar poor performance was noted in other studies,\(^{49,50}\) which reported DR for SFH well below 50%. Utilising abdominal palpation alone or in combination with SFH does not improve the detection of macrosomia, with similar DRs reported in the range of 10–43%\(^{51}\). Abdominal palpation cannot be used effectively in obese mothers as the maternal habitus makes it difficult to palpate the uterine fundus and fetal parts.

The ultrasound measurements used in clinical practice to detect LGA fetuses include abdominal circumference (AC) and a combination of measures of fetal biometry to estimate fetal weight. Older studies\(^{52-54}\) conducted in the 1980s/90s reported that ultrasound was no better than clinical examination when comparing clinical parameters with ultrasound scan for the prediction of macrosomia. However, more recent studies demonstrate that ultrasound is significantly better than SFH in predicting LGA neonates. A large multicentre study\(^{55}\) showed that ultrasound assessment of EFW detected a significantly higher proportion of LGA neonates with fetal macrosomia (more than 4000 g), based on ultrasound scan between 37 and 41 weeks of gestation, compared with SFH alone. These results are logical, despite the relatively large margin of error, as there is a degree of objectivity in assessing fetal biometry using ultrasound scan as opposed to the subjectivity of clinical examination. Although the ultrasound scan appears to perform better than other clinical estimates, the performance of screening is modest possibly due to the considerable variation in practice relating to the use of ultrasound with regards to fetal biometry measures versus AC only, and the use of different formulae, in estimating fetal weight.\(^{56-58}\) A large systematic review of 36 studies (total number of
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women 19, 117) examined the accuracy of ultrasound EFW versus AC in the prediction of macrosomia and concluded that both measures of fetal size performed equally well.\textsuperscript{56} To determine the impact of using different ultrasound formulae in estimating fetal weight, Dudley\textsuperscript{57} performed a systematic review of 11 different methods to determine the accuracy of ultrasound EFW and possible sources of error. The results demonstrated that a degree of inter- and intra-observer variation affecting the accuracy of EFW calculations with no single formula better than another. However, when the degree of error was compared between the groups that were appropriate for gestation (AGA) and those that were LGA, all formulae generally tended to underestimate EFW in the LGA population. Similar results were reported in a further study\textsuperscript{58} that examined 26 different models of fetal weight estimation in 3705 singleton pregnancies within 3 days of delivery. Although there was considerable variation between the models the estimates were generally within 15% of the actual birthweight in more than 80% of cases. Secondly, assessment of the accuracy of the models according to the birthweight categories concluded that all models overestimate fetal weight in the low birthweight category, but underestimate fetal weight in the high birthweight category. These results were similar to those reported by Dudley\textsuperscript{57} and highlight a degree of systematic error in the ultrasound estimations of fetal weight in low-risk populations; in pregnancies with LGA fetuses there is a tendency to underestimate birthweight by approximately 6%.\textsuperscript{57,58}

A more recent study\textsuperscript{23} of more than 75,000 pregnancies demonstrated that fetal macrosomia can be effectively predicted by combined screening using information from the maternal demographic characteristics and fetal biometry at 19–24, 30–34 and 35–37 weeks of gestation. It was reported that screening by maternal factors alone at 11–13 weeks of gestation detected 42% of LGA neonates (above the 95th centile) at FPR of 10%. Such identification of a high-risk group to define the a priori risk based on maternal factors is similar in performance to screening by SFH. The addition of fetal biometry increased the DR to 51%, 65% and 73% at 19–24, 30–34 and 35–37 weeks of gestation, respectively. These results provide evidence that the identification of a high proportion of pregnancies at risk of delivering a macrosomic neonate is possible with combined screening. The study also highlights that the DR in the late third trimester is superior to that in the third or second trimester, suggesting that the closer the gap between ultrasound assessment and delivery, the more accurate the antenatal prediction of macrosomia. These results were also reflected in another study\textsuperscript{59} that examined 3690 pregnancies at 30–34 weeks of gestation and 2288 at 34–37 weeks of gestation. At a FPR of 10% the DR of ultrasound EFW for LGA (95th centile or above) was 53% and 63%, respectively. These results indicate that two-stage screening in the third trimester is likely to detect a high proportion of the macrosomic neonates. A review in 2014 on fetal macrosomia proposed that a routine screening scan in the third trimester would identify women at high risk of LGA fetuses, who could then be scanned at 39–40 weeks of gestation to identify those at risk of delivering macrosomic neonates.\textsuperscript{4}

Consequently, ultrasound assessment of fetal weight is the most likely tool to use for the antenatal identification of the pregnancies at risk of fetal macrosomia.

6. **Timing and mode of delivery in pregnancies with large for gestation fetuses**

There are clear recommendations stating that an elective CS should be offered to diabetic mothers with an EFW of 4500 g or more and to nondiabetic mothers with an EFW of 5000 g or more.\textsuperscript{12–14} However, there is a lack of consensus on the management of pregnancies with macrosomic fetuses with an EFW of 4000 g or more, but less than the thresholds above.

A multicentre RCT\textsuperscript{15} involving 822 pregnancies with EFW at 95th centile or above randomised women to expectant management or IOL to determine whether the latter was associated with a reduction in risk of a composite primary outcome measure of significant shoulder dystocia, fracture of the clavicle
or a long bone, brachial plexus injury, intracranial haemorrhage, or death. There was a 70% reduction in risk of the composite outcome measure (relative risk [RR] 0.32, 95% CI 0.15–0.71) in the IOL group. There were no significant differences in the incidence of perineal tears, anal sphincter injuries, vaginal lacerations, PPH or the rate of emergency CS, although there was a small increase in the need for phototherapy in neonates in the IOL group.

Similar findings were reported in a Cochrane systematic review, in which the impact of a policy of IOL for suspected fetal macrosomia on the risk of maternal complications such as operative delivery and perineal trauma and on the risk of neonatal complications such as shoulder dystocia, birth trauma or asphyxia was evaluated. Data from four RCTs, including 1190 women with suspected macrosomia, were analysed and in the IOL group there was a 40% reduction in risk of shoulder dystocia (RR 0.60, 95% CI 0.37–0.98) and an 80% reduction in risk of fractures (RR 0.20, 95% CI 0.05–0.79), but there was no significant difference in the rate of CS, instrumental delivery, brachial plexus injury or birth asphyxia. There was an increase in the risk of third- and fourth-degree tears, but this could be estimated in only one study. In another systematic review and meta-analysis evaluating the impact of a policy of IOL versus expectant management on the rate of CS in pregnancies with suspected macrosomia in nondiabetic women, no significant difference in the risk of emergency CS or any adverse maternal or neonatal outcome, except for an 83% reduction in the risk of fractures, was reported.

The results from these studies support IOL in pregnancies with LGA fetuses, because of its association with decreased risk of shoulder dystocia and fractures, without a concomitant increase in risk of CS. The ‘Big Baby’ Trial is currently underway to investigate whether a policy of IOL at 38 weeks gestation, or soon after, in women with babies with predicted macrosomia (more than 90th customised centile of EFW) will reduce the incidence of shoulder dystocia; it is scheduled to conclude in June 2021.

7. Management of pregnancies with suspected macrosomia

The key findings regarding pregnancies with fetal macrosomia are first, a strong association with increased risks of adverse maternal and neonatal outcomes. Second, evidence from recent studies suggests that ultrasound scan is more accurate in antenatal prediction compared with clinical methods, such as measurement of SFH, especially if performed in two stages, with a routine scan at 35–37 weeks of gestation followed by a scan at 39–40 weeks of gestation in high risk women.

Third, high-quality evidence from RCTs, systematic reviews and meta-analysis of RCTs form the basis for a grade A recommendation that IOL in pregnancies at risk of delivery of a macrosomic neonate reduces the risk of complications, such as shoulder dystocia and fractures, without increasing the rate of CS. Finally, recent changes to clinical practice arising from the Montgomery ruling emphasise the need for healthcare professionals to provide women with evidence-based information to allow them to make informed choices regarding their care.

The clinical implication of these key findings is that women with risk factors for delivery of a macrosomic neonate, including a high BMI, multiparity, especially those with a history of delivery of a macrosomic neonate in a previous pregnancy, and those with either pre-existing diabetes mellitus or those that develop GDM should be identified early in pregnancy as being at high risk. The second group at high risk would be those pregnancies with LGA fetuses, either identified at a routine third trimester scan or as an incidental finding. These at-risk pregnancies should be offered an ultrasound scan at 35–37 weeks of gestation and if the fetus is found to be LGA, the scan should be repeated at 39–40 weeks of gestation to confirm the diagnosis of macrosomia. If the EFW is more than 4000 g, then women should be offered clear verbal and written information regarding the potential risks of delivery of a macrosomic neonate – for the mother and the baby. They should be informed that if the EFW in a diabetic mother is 4500 g or more (or 5000 g or more in a non-diabetic mother), an elective
CS is the preferred mode of delivery. In those with EFW of 4000 g or more, there is high-quality evidence that IOL is associated with a substantial reduction in risk of shoulder dystocia and fractures, without an increase in the risk of CS.

8. Opinion

- Fetal macrosomia is associated with significantly increased risks of maternal and neonatal complications.
- Risk factors for fetal macrosomia include a high BMI; multiparity, especially those with a previous pregnancy resulting in macromomnic neonate; and those with pre-existing diabetes mellitus or those that develop GDM.
- Ultrasound is better at predicting macrosomia than clinical methods such as SFH. A policy of screening in the third trimester of pregnancy at 35–37 weeks of gestation, followed by a repeat scan at 39–40 weeks of gestation for those that are suspected to be LGA, is likely to detect a high proportion of pregnancies that deliver macromomnic neonates.
- Women should be provided with clear evidence-based verbal and written information about the risks associated with fetal macrosomia. There should be documented discussion on the risks and benefits of various management options, including expectant management, IOL and CS, with a clear plan of care made based on this shared decision-making.

References


18. UK Supreme Court Judgment Montgomery (Appellant) v Lanarkshire Health Board (Respondent) (Scotland); 2015 [https://www.supremecourt.uk/decided-cases/docs/UKSC_2013_0136_Judgment.pdf].


60. Warwick Clinical Trials Unit. Big Baby Clinical Trial [https://warwick.ac.uk/fac/med/research/ctu/trials/bigbaby/].

61.
### Appendix I: Neonatal birthweight and corresponding gestation-dependant cut-offs

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