Management of large-for-gestational-age pregnancy in non-diabetic women

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Key content:
• Over the last two to three decades there has been a 15–25% increase in many countries in the number of women giving birth to large infants.
• Rates of shoulder dystocia and caesarean birth rise substantially at 4000 g and again at 4500 g.
• There is an increase in maternal and neonatal morbidity associated with fetal macrosomia.
• Serial measurement of fundal height adjusted for maternal physiological variables substantially improves antenatal detection.
• Sonographic assessment of fetal weight is frequently inaccurate.
• Induction of labour for suspected macrosomia in non-diabetic women has not been shown to reduce the risk of caesarean section, instrumental delivery or perinatal morbidity.

Learning objectives:
• To identify the risks associated with fetal macrosomia and to be aware of the long-term implications.
• To understand the limitations of predictive tools.
• To be able to take an informed approach to managing the macrosomic fetus.

Ethical issues:
• To what extent should the fear of medico-legal action influence obstetricians’ management of suspected fetal macrosomia?
• What advice should clinicians give women regarding modes of delivery?

Keywords birth weight / estimated fetal weight / induction of labour / macrosomia / shoulder dystocia
Introduction

There has been a rise in the prevalence of large newborns in many parts of the world. Over the last two to three decades, an overall 15–25% increase in the proportion of women giving birth to large infants has been documented in the USA, Canada, Germany, Scotland and Denmark. This trend has been attributed to increases in maternal height, body mass, gestational weight gain and diabetes; reduced maternal cigarette smoking; and changes in sociodemographic factors. The prevalence of liveborn infants weighing >4000 g was 11.65% in our institution (Wycombe Hospital, UK) in 2008. It is known that there is an increase in maternal and neonatal morbidity associated with fetal macrosomia. However, there is no universal consensus on the definition, diagnosis and antenatal management of fetal macrosomia. In this review, we try to provide a sensible approach to management of large-for-gestational-age (LGA) pregnancies in non-diabetic women based on the available evidence.

Search strategy

Electronic searches of literature published between 1980 and 2009 were undertaken using MEDLINE, Embase, CINHAL, the Cochrane Database of Systematic Reviews and the National Institute for Health and Clinical Excellence (NICE) website. Search items included: pregnancy, fetal macrosomia, foetal macrosomia, macrosomic fetus, large for dates, large for gestational age and macrosomia, combined with the terms non-diabetic, brachial plexus injury, shoulder dystocia, antenatal care, perinatal care and management. Terms were connected by the Boolean operator ‘OR’. This retrieved a total of 312 references and, after exclusion of duplicate and obviously irrelevant papers, 60 studies published in the English language or with an English language abstract were identified.

Terminology

The term large-for-gestational-age has mainly been used for fetuses or newborns with an (estimated) weight >90th percentile or >2 standard deviations from the mean for the gestational age. The Ponderal Index is an indicator of body proportions, which are determinants of short-term obstetric complications and long-term health problems. In this article, we will define LGA fetuses as those with an (estimated) birth weight >4500 g.

Risk factors and obstetric complications associated with macrosomia

In an American cohort study, Stotland et al. identified the risk factors associated with neonatal birth weight >4500 g. Male infant sex, multiparity, maternal age 30–40 years, white race, diabetes and gestational age >41 weeks appeared to be associated risk factors (P < 0.001). Adverse obstetric outcomes were also studied in this cohort. Women who delivered a macrosomic infant were more likely to undergo caesarean birth and to suffer shoulder dystocia, chorioamnionitis, fourth-degree perineal lacerations, postpartum haemorrhage and longer hospital stay. Adjusted odds ratios (ORs) for caesarean birth of birth weight groups 4000–4499 g, 4500–4999 g and ≥5000 g were 1.69, 2.99 and 5.46; and for shoulder dystocia were 6.29, 13.05 and 17.52, respectively. Limitations of this study are secondary data analysis, lack of data on confounding factors and the study group being a cohort of privately insured patients.

On the other hand, the evidence showed no differences in adverse birth outcomes between birth weights of 3500–3999 g and those of 4000–4499 g. High birth weight (4500–4999 g) and very high birth weight (≥5000 g) were found to be associated with early neonatal death; the leading cause of death was asphyxia. The majority of post-neonatal deaths were caused by sudden infant death syndrome. Very high birth weight infants were twice as likely to die of sudden infant death syndrome as normosomic infants, whereas high birth weight infants were not at increased risk. The risk of shoulder dystocia rises from 1.4% for all vaginal deliveries to 9.2–24% for birth weights >4500 g.

The American College of Obstetricians and Gynecologists defines macrosomia as birth weight >4500 g, irrespective of gestational age, as both maternal complications and perinatal morbidity and mortality begin to rise from that birth weight.

Long-term health risks

Meta-analysis of the 14 studies that examined the association between birth weight and risk of type 2 diabetes in later life showed a U-shaped association. Low birth weight (<2500 g) and high birth weight (>4000 g) were associated with increased risk of type 2 diabetes. Size at birth, particularly length and head circumference, is associated with increased risk of breast cancer in premenopausal women.
women after adjustment for adult risk factors and birth weight. A population-based cohort study by Sin et al. determined the relationship between birth weight and risk of emergency visits for asthma during childhood. Those with a high birth weight had a significantly increased number of visits and the relationship was linear if birth weight was >4500 g, such that every increment of 100 g in birth weight was associated with an additional 10% increase in the risk of emergency visits. A number of very large, well-conducted studies have shown an association between birth weight and subsequent body mass index (BMI) (kg/m²) or overweight, at least for young white adults and children. By contrast, several studies have shown no association in middle-aged subjects, although these were fairly small studies. Genetic factors were predominant in this association, especially with BMI in adulthood.

Diagnosis of fetal macrosomia

(See Figure 1.) Clinical estimations are based on palpation of the uterus and measurement of the height of the fundus of the uterus; both are subject to considerable variation.

Fundal height measurements are an inaccurate way of estimating fetal size. They are influenced by the maternal size, amount of amniotic fluid, status of the bladder, pelvic masses (e.g. fibroids), fetal position and many other factors. Serial measurements of fundal height adjusted for maternal physiological variables such as age, weight, height, ethnicity, parity and birth weight in previous pregnancies, significantly increase the antenatal detection of LGA babies (the detection rate was 46% in the study group compared with 24% in the control group; OR 2.6; confidence interval [CI] 1.3–5.5). This is followed by fewer investigations and, hence, is a cost-effective screening tool for fetal growth in the community. To improve assessment of fetal growth it is critical that the measurements are taken serially rather than done as a one-off measurement.

Ultrasoundographic prediction of fetal macrosomia

Ultrasound measures used for predicting a macrosomic fetus are either single parameters (such as abdominal circumference or subcutaneous tissue thickness) or combinations of measurements to estimate fetal weight. Ultrasound biometry used to detect fetal weight >4000 g is characterised by low sensitivity, low positive predictive value and high negative predictive value.

Figure 1
Algorithm for the diagnosis of LGA pregnancy in non-diabetic women. At all stages of management, it is crucial to obtain the woman’s agreement.

Clinically LGA at 36 weeks of gestation by palpation

SFH >90th centile confirmed on personalised growth chart

Ultrasound biometry, including AFI

EFW >90th centile and increased AFI

Check glucose in urine, GTT at booking visit, previous history of gestational diabetes mellitus

Increased AFI or glucose in urine

Arrange GTT

Normal GTT

Follow primiparous or multiparous pathway (Figure 2 and Figure 3)

Abnormal GTT

Refer to diabetes team

AFI = amniotic fluid index; EFW = estimated fetal weight; GTT = glucose tolerance test; SFH = symphysio-fundal height.
A systematic quantitative review of 63 accuracy studies\(^{19}\) (which included 51 evaluating the accuracy of estimated fetal weight [EFW] and 12 evaluating the accuracy of fetal abdominal circumference, including a total of 19,117 women) assessed ultrasonographically-estimated fetal weight and abdominal circumference in the prediction of macrosomia. The summary receiver operating characteristic curve (sROC) area for EFW was not different from the area for fetal abdominal circumference (0.87 versus 0.85, \(P = 0.91\)), suggesting that there was no difference in accuracy between ultrasonographically-estimated fetal weight and abdominal circumference in the prediction of a macrosomic baby at birth. For predicting a birth weight of \(>4000\) g, the summary likelihood ratios (LRs) were 5.7 (95% CI 4.3–7.6) for a positive test and 0.48 (95% CI 0.38–0.60) for a negative test, using Hadlock et al.’s formula of estimating fetal weight ultrasonographically.\(^{24}\)

For ultrasound fetal abdominal circumference of 36 cm, the respective LRs for predicting birth weight \(>4000\) g were 6.9 (95% CI 5.2–9.0) and 0.37 (95% CI 0.30–0.45). A positive test result is more accurate at ruling in macrosomia than a negative test result at ruling it out.\(^{25}\)

Similarly, ROC curves indicated that measurements of soft tissue are not superior to clinical or other sonographic predictions in identifying fetuses with weights of \(>4000\) g, although the study had limited power.\(^{26}\)

Combinations of amniotic fluid index and EFW measurements during the middle of the third trimester are useful predictors of macrosomia at birth. Combined analysis of amniotic fluid index \(\geq 60\)th percentile and EFW \(\geq 71\)st percentile resulted in a positive predictive value of 85%,\(^{27}\)

Several studies\(^{22,28}\) have compared clinical with ultrasound estimation of birth weight and none of these have demonstrated ultrasound to be superior to clinical estimation. Both clinical and sonographic predictions of macrosomia include areas of the ROC curve between 0.81 and 0.95, which is defined as useful from a statistical point of view. However, predictions of macrosomia by these techniques are limited by the substantial false-positive and false-negative rates inherent in these tests.\(^{29}\)

There are some studies that suggest ways to improve the predictive accuracy of fetal macrosomia. Serial sonographic measurements can increase the positive predictive value.\(^{30}\) However, serial biometry is time consuming and the cost effectiveness is questionable. Regardless of the formula used, the accuracy of sonographic estimates decrease with increasing birth weight.\(^{31}\) Three-dimensional ultrasound and magnetic resonance imaging (MRI) are expected to be additional tools in future to estimate fetal weight and even body composition, but their usefulness needs to be further investigated.\(^{32,33}\) A software program (a customised fetal growth chart) that calculates on the basis of pregnancy variables entered at the first visit provides an adjusted normal range for that particular fetal size and is, thus, more specific. Using the program, 22% of those designated large (\(>90\)th centile) on the standard population growth chart were within normal limits for the pregnancy. Conversely, 26% of babies identified as large, with adjusted centiles, were ‘missed’ by conventional unadjusted centile assessment. Adjustment for physiological variables makes assessment of fetal growth more precise and reduces unnecessary interventions and parental anxiety.\(^{34,35}\) Similarly, computerised combinations of a number of risk factors such as diabetes and twin pregnancy may also improve identification of macrosomia.\(^{36}\)

### Other predictors of macrosomia

A change in maternal BMI during pregnancy has an independent positive predictive value for fetal macrosomia. An increase in BMI \(\geq 25\)% during pregnancy has a sensitivity of 86.2%, specificity of 93.6%, positive predictive value of 71.4% and negative predictive value of 97.45% for macrosomia.\(^{37}\)

Women with a history of one macrosomic infant are at significantly increased risk of another macrosomic infant in a subsequent pregnancy. For women with two or more macrosomic infants, the risk is even greater.\(^{38}\)

### Management

Management of pregnancies with suspected fetal macrosomia (Figure 2, Figure 3 and Box 1) is challenging for clinicians. Elective caesarean section is intended to prevent several of the complications associated with fetal macrosomia, especially brachial plexus injuries and maternal perineal lacerations. However, it has been estimated that \(>3600\) caesarean deliveries need to be performed in non-diabetic women with suspected fetal macrosomia (\(\geq 4500\) g) to prevent a single permanent brachial plexus injury.\(^{39}\) Thus, elective caesarean section for the sole indication of macrosomia cannot be justified.

Clinical research, in conjunction with cost-effectiveness analyses, has led to the consensus that elective caesarean delivery is only beneficial for non-diabetic women whose fetus is suspected to be \(\geq 5000\) g.\(^{40}\)

Before caesarean section became reasonably safe, induction of labour for suspected macrosomia was
performed because it was thought to prevent problems from severe cephalopelvic disproportion and its associated maternal mortality and severe morbidity. Nowadays, many obstetricians induce labour at term when the fetus is estimated to be either LGA or macrosomic.

A meta-analysis of systematic review on 11 studies by Sanchez-Ramos et al.\(^3\) compared the outcomes of expectant management with labour induction in women with suspected fetal macrosomia. Based on data from nine observational studies, labour induction for suspected fetal macrosomia results in an increased caesarean delivery rate without improving perinatal outcomes. However, two randomised controlled trials have not confirmed these findings, although their statistical power is limited.

Similarly, according to Irion and Boulvain,\(^4\) compared with expectant management, induction of labour for suspected macrosomia in non-diabetic women has not been shown to reduce the risk of caesarean section or instrumental delivery. Perinatal morbidity (shoulder dystocia) was not significantly different between groups.

Thus, current evidence shows no benefit of a policy of routine induction of labour at the mere indication of suspected fetal macrosomia (\(>4000\) g).

From the retrospective case-controlled study by Ben-Haroush et al.,\(^5\) induction of labour for suspected LGA fetuses increases the risk of caesarean section, confirming the results of previous studies. However, within the subgroup of

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### Figure 2
Algorithm for antenatal management of LGA pregnancy in non-diabetic primiparous women. At all stages of management, it is crucial to obtain the woman’s agreement

<table>
<thead>
<tr>
<th>No further scans after 36 weeks</th>
<th>Maternal BMI, cervical assessment at 41 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt;30, favourable cervix</td>
<td>Induction of labour at 41(^{st}) weeks</td>
</tr>
<tr>
<td>BMI &gt;30, unfavourable cervix</td>
<td>Consider elective lower segment caesarean section or induction of labour</td>
</tr>
</tbody>
</table>

### Figure 3
Algorithm for antenatal management of LGA pregnancy in non-diabetic multiparous women. At all stages of management, it is crucial to obtain the woman’s agreement

<table>
<thead>
<tr>
<th>No further scans after 36 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous history of macromomia, vaginal delivery, no birth injuries</td>
</tr>
<tr>
<td>Induction of labour at 41(^{st}) weeks</td>
</tr>
<tr>
<td>Previous caesarean section</td>
</tr>
<tr>
<td>Previous vaginal delivery or indication for caesarean section not failure to advance, and/or BMI &lt;30</td>
</tr>
<tr>
<td>No previous vaginal delivery; or previous caesarean section indicated by failure to advance; and/or BMI &gt;30</td>
</tr>
<tr>
<td>Vaginal birth after caesarean section</td>
</tr>
<tr>
<td>Consider elective lower segment caesarean section</td>
</tr>
<tr>
<td>Induction of labour at 41(^{st}) weeks and short trial of labour</td>
</tr>
<tr>
<td>Elective lower segment caesarean section</td>
</tr>
</tbody>
</table>

### Box 1
Management in labour of women with LGA pregnancy

**First stage**
- Intravenous line, group and save
- Continuous cardiotocograph monitoring
- Adequate pain relief
- Regular cervical assessment, especially of descent of the presenting part
- Timely augmentation with oxytocin if delay in the first stage is diagnosed

**Second stage**
- Early recourse to caesarean section if there is no descent of the presenting part
- Delivery by a senior midwife
- Obstetric registrar or consultant in attendance

**Third stage**
- Active management of third stage and administration of Syntometrine® (Alliance) (ergometrine and oxytocin) by injection
multiparous women, caesarean section rates were not increased, with no major maternal or fetal complications, showing that nulliparity was significantly and independently associated with increased risk of caesarean section.

A holistic approach should be taken in the management of pregnant women. Important variables such as women's age, height, BMI, parity, birth weights of previous babies and obstetric history, including previous shoulder dystocia and cervical score, should be considered in the decision-making process.

Based on an analysis of treatment of suspected fetal macrosomia, expectant treatment is the most cost-effective approach. In a large cohort studied by Walsh et al., 88% of women who laboured with a macrosomic infant achieved vaginal delivery. If expectant management is decided upon, the woman should be fully informed about the benefits and possible consequences, including care during labour.

An observational study carried out by Draycott et al. demonstrated that the introduction of shoulder dystocia training for all maternity staff was associated with improved management and neonatal outcomes of births complicated by shoulder dystocia.

During labour, regular assessment of progress is required, especially of engagement, descent and rotation of the fetal head. Continuous electronic monitoring of the fetal heart rate should also be performed because of the increased oxygen requirement of the macrosomic fetus and the association with prolonged labour. Thorough second stage assessment is crucial if it is prolonged, in order to avoid forceful extraction by instrumental delivery. A competent obstetrician must be in attendance to handle shoulder dystocia promptly and effectively. Moreover, a paediatrician should be present at the time of delivery, since hypoxia and other injuries may be expected. Active management of the third stage of labour should be exercised to avoid postpartum haemorrhage.

Management of fetal macrosomia in special circumstances

Previous caesarean section

The medical literature does not support elective caesarean section for suspected fetal macrosomia in non-diabetic women and there appears to be no reason for treating mothers with previous caesarean sections differently.

There is still a very low threshold for elective caesarean section in non-diabetic pregnant women with a birth weight of ≥4000 g. One in four non-diabetic pregnant women with a birth weight ≥4000 g underwent elective caesarean section with the indication of ‘one previous caesarean section with large for date’ in our institution (unpublished retrospective audit from 1 January 2008 to 30 June 2009).

Strong predictors of success of vaginal delivery are: previous vaginal birth, indication for previous caesarean delivery and maternal BMI. Previous vaginal birth predicted the success of trial of vaginal births in women with macrosomic fetuses. Maternal obesity is an independent risk factor for failed trial of labour in women with previous caesarean sections.

Previous shoulder dystocia

Women (with or without diabetes) with previous shoulder dystocia have an increased risk of recurrence, ranging from 1.1–16.7%. In non-diabetic women, there is insufficient evidence to support routine elective delivery; however, the contrary applies to those cases complicated by permanent brachial plexus injury. A thorough review of previous delivery records is necessary.

Shoulder dystocia seldom results in brachial plexus injury. Most injuries are transient; half the cases of shoulder dystocia occur in infants with birth weights <4000 g and approximately one-third of brachial plexus injuries are not even associated with a clinical diagnosis of shoulder dystocia. As many as 50% of all brachial plexus injuries are attributable to unavoidable intrapartum or antepartum events. They can, therefore, occur through mechanisms other than the efforts exerted to reduce an impacted shoulder. This implies that the mode of delivery does not have a major impact on the incidence of injuries in about 40% of women experiencing brachial plexus injury. In fact, brachial plexus injury has been reported even after caesarean delivery. Thus, caesarean delivery reduces but does not eliminate the risk of birth trauma associated with macrosomia.

Conclusion

The widespread availability of obstetric ultrasound and the fear of medico-legal action due to shoulder dystocia have led obstetricians to consider interventions for ultrasonographically diagnosed macrosomia. We have found no evidence to support a policy of induction of labour or routine elective caesarean section of non-diabetic women with ultrasonographically diagnosed LGA pregnancies if the EFW is <5000 g. However, there is evidence to support elective caesarean section for women with EFW ≥5000 g.
References


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