BIG BABIES, BIG PROBLEMS? FETAL MACROSOMIA

Clinical variables and maternal and

perinatal outcome associated with mode of delivery.

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DECLARATION

I Gabrielle Dominique Toweel declare that this research project is my own work. It is being submitted in partial fulfilment for the Masters in Medicine (MMed) in Obstetrics and Gynaecology.

Dr G D Toweel **Date:**

ABSTRACT

Objectives

- To determine the prevalence of macrosomic babies delivered at Coronation (now Rahima Moosa) Hospital.
- To compare the maternal and neonatal outcome of vaginally born macrosomic babies versus vaginally born babies less than 4000g.
- To determine the impact that mode of delivery of the macrosomic babies had on maternal and neonatal outcome.
- To compare clinical variables for macrosomia with those published in the literature, in view of identifying predictive factors.

Method

Retrospective record review of all women who delivered at Coronation (Rahima Moosa) Hospital from 1 January 2005- 30 June 2005.

Results

A total of 134 macrosomic infants were identified, of which 76 were delivered vaginally, 14 by elective caesarean section and 44 by emergency caesarean section. During the study period, there were 5800 deliveries. The incidence of macrosomia in the study population was 2.3%. Characteristics specific to the

cohort of macrosomic infants revealed that male sex was more common (52/74 (70%) in the macrosomic group vs. 32/74 (43%) in the non-macrosomic group, $p<0.0009$), length of labour was increased (13.7 vs. 10.9 hours, $p=0.032$), as was use of augmentation (16 vs. 5, $p=0.009$), perineal trauma (34 vs.19, $p=0.010$) post partum haemorrhage (10 vs.2, $p=0.016$) and shoulder dystocia (5 vs. 0, $p=0.03$). Vaginal delivery, compared to elective or emergency caesarean section resulted in less fetal distress (1 vs. 13, $p<0.0001$) and puerperal fever (4 vs. 19, $p=0.0001$). Differences in other fetal and maternal outcomes were not significant.

Conclusion

Fetal macrosomia was more likely to be associated with advanced gestational age, male sex, prolonged labour, post partum haemorrhage, use of augmentation, increased perineal trauma especially episiotomy and shoulder dystocia .

Expectant management, progressing labour according to a standardized partogram and no elective caesarean section on the basis of clinical and or ultrasound diagnosis of an increased estimated fetal weight, appears to be the best form of management for the suspected macrosomic.

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BIG BABIES, BIG PROBLEMS?

FETAL MACROSOMIA:

Clinical variables and maternal and perinatal outcome associated with mode of delivery.

1 BACKGROUND

As birth weight increases, the likelihood of labour abnormalities, including shoulder dystocia, birth trauma and permanent injury to the neonate, increases. Adverse maternal outcomes also increase, for example post-partum haemorrhage, perineal trauma and obstructed labour, as does the use of augmentation.[1, 2] Fetal macrosomia can result in other serious complications such as perinatal asphyxia, meconium aspiration, labour disorders and high incidence of caesarean section. Antenatal diagnosis of macrosomia could possibly decrease perinatal morbidity,[3] although prenatal recognition of overgrown fetuses is often difficult because less than 40% are born to patients with identifiable risk factors.[1, 2] The optimal mode of delivery and labour management of these patients is debateable and largely uncertain.

This study was performed to gain a South African perspective on macrosomia.

2 INTRODUCTION

The concept of fetal macrosomia and its adverse outcomes has been recognised in medicine and literary reports throughout the ages. The 16th century monk and physician, Francois Rabelais, told the story of the birth of Gargantua, a 'giant' baby. Several years later, Gargantua's wife died giving birth to Pantagruel, "for he was so amazingly large and so heavy that he could not come into the world without suffocating his mother".[4] In 1891 Ortega reported the birth of a 24-pound, 13-ounce male infant and Belcher, in 1916, claimed to have delivered the largest infant, a 25-pound stillborn.[4]

Fetal growth is exponential and during the last 20 weeks of gestation the fetus gains 95% of its weight. Genetic, nutritional, environmental, uteroplacental, and fetal factors have been suggested to influence fetal growth. Uteroplacental and umbilical blood flow and transplacental glucose and fetal insulin are major determinants of fetal growth. The role of the fetal pituitary (growth hormone) and thyroid gland in fetal growth is not well understood; human anencephalic or athyroid fetuses usually have no or only minor retardation of growth. Also, it is not clear whether placental lactogen or somatomedin or a somatostatin-like substance of the placenta and fetus influences fetal growth. From experiments on rats it may be assumed that a specific placental-fetal growth-promoting and growth-regulating factor(s) exists. Identification of such a placental-fetal growth factor(s) in humans might aid in the prevention, diagnosis, and treatment of fetal growth retardation. [5]

While investigating growth factors and regulation of fetal growth, Hill et al discovered that fetal growth demands a coordinated increase in size of the fetus and the placenta, both of which are determined, in part, by locally produced peptide growth factors. The availability of growth factors to individual tissues may be due to local changes in gene expression, but it is also controlled by proteolytic release from extracellular matrix stores. Members of the fibroblast growth factor (FGF) family are stored within basement membranes, while insulin-like growth factors (IGFs) are stored in association with specific binding proteins (IGFBPs). Insulin is a major trophic hormone in utero, and pancreatic beta-cell mass is determined by locally produced IGF-II and members of the FGF family. The mitogenic effects of IGF-II on beta-cells are determined by IGFBPs, which are themselves expressed with a distinct ontogeny within the islets of Langerhans. FGF-2 is also widely expressed within fetal tissues and may be an important regulator of placental angiogenesis. FGF-2 appears in the maternal circulation during pregnancy, with peak values late in the 2nd trimester. It is associated with a circulating binding protein derived from the extracellular domain of the FGFR1 receptor. Levels of FGF-2 in maternal serum correlate positively with fetal size, both in the 2nd trimester and at term. The expression of FGF-2 in placenta and its presence in maternal blood are elevated in pregnancies complicated by diabetes and are greatest in diabetic pregnancies associated with retinopathy. Maternal FGF-2 may thus be a useful indicator of both fetal development and the risk of maternal pathology in pregnancies complicated by diabetes.[6]

Insulin is the only fetal hormone related to intrauterine growth. Maternal insulin cannot diffuse through the placental membrane and therefore insulin is derived from the fetus. Clinical and experimental evidence has indicated that insulin can be considered the true fetal growth hormone. There is a positive correlation between plasma insulin levels and fetal weight in a significant number of animal species. High levels of insulin infusion resulted in a 10-25% rate of change in weight in monkeys and rats. Intrauterine growth retardation had been reported in full term neonates with pancreatic agenesis. Insulin has a significant role in postnatal life as an anabolic hormone, mainly in carbohydrate metabolism. In fetal growth, insulin is the most recognized regulatory hormone. The fetal pancreas is the only source of insulin in the fetal circulation and is already present at 8-10 weeks gestation. It remains relatively inactive until 20 weeks of gestation, when the insulin response to glucose becomes evident. The insulin response to exogenous glucose is related to the endogenous glucose levels in fetal circulation, which mandate the sensitivity of the fetal beta cells. Thus chronic fetal hyperglycemia accelerates the development of insulin secretory mechanisms predisposing infants of mothers with diabetes to have a mature insulin response.[4.]

The role of thyroid hormone and growth hormone in postnatal growth is well established, but these hormones appear to have a minimal role in prenatal growth. Adrenal corticosteroids fulfil a critical role in the induction of maturational processes in specific organ systems such as the lung and intestine. The influence

of growth hormone on regulation of fetal growth is negligible. This may be related to the absence of growth hormone receptors in the fetal liver. [4.]

In fetal macrosomia, the fetal growth pattern and type of tissue overgrowth reflects the underlying aetiology. Insulin-sensitive tissues, such as the heart, liver and spleen, thymus, adrenal gland, subcutaneous fat, and shoulder girdle, can show differential glycogen and fat deposition when insulin levels are high. As a result, total body fat, shoulder and upper-extremity circumference, upper-extremity skin-fold thickness, and liver size are disproportionately greater in macrosomic infants of diabetic women compared with those of women without diabetes. [7,8] These differences in growth patterns are at least partially responsible for the significant associated fetal, neonatal, and maternal risks. [9]

Macrosomia is arbitrarily defined as having a fetal weight of above the 90th percentile for the expected gestation, a birth weight of above 4000g or 4500g or a birth weight of over +2 standard deviation of the mean birth weight by gestational age.[10] Fetal macrosomia may be defined using a relative or absolute scale,[1] but when arbitrarily defined, it is a birth weight of more than 4000g. Fetal macrosomia complicates more than 10% of all pregnancies in the United States [11] and is associated with increased risks of caesarean section,[12] induction of labour, operative delivery, obstructed labour and trauma to the birth canal and the fetus.[13]

The prevalence varies substantially across different continents, namely <3% in Nigeria, Pakistan, Thailand, and Taiwan but ≥ 20% in Denmark and the Republic of Croatia.[14] A study by Essel et al, which had an African perspective to it, examining the incidence of macrosomia in the black African population attending Umtata General Hospital, reported an incidence of 3.43% of all singleton deliveries.[15] Buchmann in his study of the population in the Chiawelo district of Soweto, calculated the incidence of fetal macrosomia to be 2.3%.[16]

As was noted previously, triggers for fetal growth appear to be both genetic and environmental. [17] When evaluating risk factors for macrosomia or excessive fetal growth, Wallace et al found the initial drive to be genetic with male genotype and Caucasian ethnicity being risk factors for increased fetal size [17], but they like many others also found that environmental risk factors also play a role. These include a negative smoking history, gestation >40 weeks and the presence of maternal diabetes (both pre-pregnancy and gestational). [17]

A number of other risk factors for fetal macrosomia are widely recognized, including increased age, maternal pre-pregnancy weight, maternal impaired glucose intolerance, multiparity, previous macrosomic infant, excessive weight gain during pregnancy, parental stature (height) [13] and high maternal birth weight[1, 12,30] The strongest risk factor is maternal diabetes which results in a twofold increase in the incidence of macrosomia. Clausen et al in their study of maternal

anthropometric and metabolic factors in the first half of pregnancy and risk of neonatal macrosomia in term pregnancies also found that among other factors first trimester BMI, gestational weight gain and placental weight were associated with macrosomia. High serum insulin levels, high levels of the non-high density lipoprotein (HDL) cholesterol and low serum HDL cholesterol were associated with an increased risk of macrosomia independent of BMI, weight gain, placental weight and gestational diabetes. Interestingly they found that slim women with macrosomic infants had higher insulin compared with those with normal weight infants. The same did not hold true among obese women. Studies using leptin levels found no positive associations with macrosomia. [18]

The incidence of macrosomia is on the rise, and many are speculating as to the cause of this increased prevalence of macrosomia in certain countries over the last decade. Most ascribe this to the alarming increase in obesity as well as type 2 diabetes in affluent countries.[19] Fraser in his article outlines the influence of maternal obesity on fetal growth. He suggests that the excess substrate provision across the placenta due to an increase in fasting plasma glucose levels associated with maternal obesity have a direct effect on fetal growth.[19] In their unit, Fraser et al, cultured trophoblast cells for term placentas of women with diabetes and showed a direct correlation in the uptake of both amino acids and glucose with increasing birth weight. These studies suggested that when the feto-placental unit is confronted by an excess availability of maternal substrates, placental transport mechanisms for these substrates are upregulated. There is no evidence to show

that the fetus can protect itself from the negative effect of this excess glucose and amino acid transfer across the placenta. [20] Most literature suggests a strong relationship between maternal obesity and fetal macrosomia. [21]

The Pedersen hypothesis explains how maternal diabetes stimulates fetal growth.[17] Maternal hyperglycaemia leads to an elevation in fetal glucose levels, which in turn causes overstimulation of the fetal pancreas and fetal hyperinsulinaemia. Insulin has many growth promoting properties and the resulting fetal hyperinsulinaemia therefore stimulates increased fetal growth. This is particularly apparent in the third trimester.[17]

It is evident that many of these risk factors (e.g. prolonged gestation, obesity and multiparity) are highly prevalent among pregnant women; this may therefore limit their utility, as even when two or more of these risk factors are present, the risk of fetal macrosomia is only 32%. Therefore, 34% of macrosomic infants are born to mothers without any risk factors and 38% of pregnant women have at least one risk factor.[12] Excessive birth weight is associated with higher maternal pregnancy weight gain as well as maternal obesity, both of which have increased over the past two decades.[1,6,14]

In the United States approximately 10% of infants have a birth weight of 4000g or more and 1.5% weigh at least 4500g, with over 12% of women gaining 46lb (20.9kg) or more during their pregnancy in 2000 versus 9.1% a decade earlier.[11] In a large cohort of >146 000 privately insured patients in the US, macrosomia was more common in this population than in the general US population, and within the cohort, advanced gestational age, white race and maternal age 30-39 were significant risk factors for macrosomia.[11] Women delivering macrosomic infants had an increased number of adverse outcomes,[22] including increased caesarean birth, shoulder dystocia, chorioamnionitis and post partum haemorrhage.[11-13] Vaginal delivery of a macrosomic infant has also been found to increase the risk of third and fourth degree lacerations fivefold.[12]

The most feared and problematic outcome of macrosomia is shoulder dystocia,[23] where up to one fourth of infants with shoulder dystocia experience brachial plexus or facial nerve injuries or fractures of the humerus or clavicle.[12] However, regardless of birth weight, most infants born after deliveries complicated by shoulder dystocia do not have brachial plexus injury.[4] Birth asphyxia, albeit rare, is also a feared complication that may occur secondary to shoulder dystocia.[12]

There are other neonatal morbidities associated with macrosomia including neonatal hypoglycaemia, other neonatal metabolic abnormalities and an increased lifetime risk of developing diabetes, hypertension, and cardiovascular disease.[1]

Barker's hypothesis, named after David J Barker, a researcher at the University of Southhampton, states that reduced fetal growth is strongly associated with a number of chronic conditions later in life. [24] This increased susceptibility results from adaptations made by the fetus in an environment that was limited in nutritional supply. Chronic conditions that can occur as a result include coronary heart disease, stroke, diabetes and hypertension.[24]

When analysed in relation to maternal obesity and diabetes, Fraser et al imply a similar concept to this hypothesis where they show that the fetal hypertrophy associated with maternal obesity is a trigger for obesity in childhood and probably in adult life also.[20]. Many other studies echo these sentiments where an association with fetal macrosomia and long term health problems, including an increased risk of obesity in adolescence and diabetes in later life and an increased rate of certain childhood cancers have been reported. [17,19.]

Fetal macrosomia is however, extremely difficult to predict antenatally with 3 possible major strategies being used to estimate foetal weight and therefore foetal macrosomia, namely: clinical risk factors, clinical estimation and ultrasonography.[3,12,25.]

The American College of Obstetricians and Gynaecologists (ACOG) [26] in their guidelines acknowledge the difficulty of estimating fetal weight and recommend

Leopold's maneuvers and measurement of the height of the uterine fundus above the maternal symphysis pubis as the two primary methods used for clinical estimation of fetal weight.[26] Nahum et al in their study drew similar conclusions regarding the using of Leopold's maneuvers in predicting fetal weight. [27.] They compared results obtained from medical students and house staff physicians estimating fetal weight at term using this technique. Their findings were that house staff physicians performed significantly better than medical students and were able to predict fetal weight within 10% of the actual birth weight in 71% of cases vs. 38% in the medical students group. This was presumably due to their increased experience in using these tactile techniques. In their study the mean birth weight was 3.445kg +- 458g and the range was 2.485-4.790kg.[27.]

Clinical and ultrasonographic estimates of fetal weight are prone to error.[12] Several studies which analysed antenatal detection of macrosomia have focused on the accuracy of ultrasonic estimation of fetal weight using various formulas.[23] Shepard et al in the early 1980's developed and revised a formula that they used to successfully predict fetal weight within 10% of the actual fetal weight. The formula is as follows Log 10 (birth weight) = -1.7492 + 0.166/(BPD) + 0.046(AC)-2.646 (ACxBPD) / 1.000.[28] Nahum et al suggested that using a new and rather complex combination algorithm in sophisticated bioinformatics-processing systems, fetal macrosomia could be accurately predicted before delivery. An example of this equation is 'birth weight= -1627+(13.18x fetal AC [mm])+(16.23xUS to delivery interval[days])+(0.00009964x gestational age[days] x maternal height[cm] x 26 wk

maternal weight [kg]) +(3.173x gestational age[days] x maternal weight gain rate[kg/day] x [parity +1])[2,29] This is in contrast to many studies which have failed to identify an accurate method of estimating fetal weight, especially by means of ultrasound alone[30] and suggest that clinical estimation of fetal weight still plays a vital role in modern day medicine [23,31] and that ultrasound estimation is often too heavily relied upon.[23]

Chauhan et al looked at the limitations of clinical and sonographic estimates of birth weight comparing pregnancies throughout the third trimester and they found that sonographically estimated fetal weight was only more accurate than clinical estimations in preterm and not in term or post term pregnancies. This study was limited to fetal weights >500g and <4500g.[32] In a study on estimate of birth weight in term parturients, clinical estimation had significantly higher accuracy than those derived sonographically. (58% vs. 32% within 10% of actual birth weight) [33].

Accurate weight estimation in fetal macrosomia appears to be much more limited and unsuccessful. When Hart et al tried to determine which formula best predicts fetal weights above 4000g, their results confirmed earlier reports that weight prediction in fetal macrosomia tended to be inaccurate.[34]. They concluded that few of the commonly applied formulas could reliably predict birth weight and suggested that new methods of estimating fetal weight in fetuses weighing >4000g are

required, where three dimensional volumetry may be an option. [34]. Schild et al evaluated the accuracy of three dimensional ultrasound in fetal weight estimation and they confirmed the superior role of 3D ultrasound in estimating fetal weight close to delivery with much smaller margins of error, i.e. mean error of 25.8g+-194.4 vs. 107.8g+-272.7 using Hansmanns' formula.[35]. Hansmanns formula is estimated fetal weight =-0.001665958 x abdominal transverse diameter3 in centrimetres (ATD)+ 0.4133629 x ATD2 – 0.5580294 x ATD – 0.01231535 x biparietal diameter 3 in centimetres(BPD) + 3.702 x BPD2-330.1811 x BPD – 0.4037199 x GA3 + 55.958061 x GA2 – 2,034.3901 x GA x 32,768.19.[36] The use of 3D estimation at the extremes of fetal weight still needs evaluation.[35] Hackmon et al evaluated a combined analysis of amniotic fluid index(AFI) and estimated fetal weight (EFW) in the mid third trimester and found an AFI>= 60th percentile and an EFW >=71st percentile during the mid third trimester are useful predictors of severe macrosomia at birth.[37] Hackmon et al in another innovative study questioned whether severe macrosomia could be determined at the time of nuchal translucency screening. Although it was a small study group of only 20 term macrosomic newborns being compared to 67 appropriate for gestational age newborn controls, they found that fetal biometry at the time of the nuchal translucency screening was statistically higher in the macrosomic newborns when compared to controls(2.65 +-2.06 days vs. 0.68 +-1.4 days, p=0.001). [38] More studies are necessary, but findings from this small study suggest that some cases of fetal macrosomia express themselves as early as 11-14 weeks gestation.[38]

The American College of Obstetricians and Gynecologists introduced a third, poorly investigated method to identify a macrosomic fetus. This involves asking a parous patient, based on their experience from a previous pregnancy to approximate the weight of their term fetus [3,9,17] Based on this hypothesis, Jolly et al (2003) concluded that in the multigravidae, the maternal estimate of fetal weight may be as accurate as ultrasound prediction.[13]

Chauhan et al also found that maternal estimates of birth weight were more accurate than clinical estimates of ultrasound, namely almost 70% of estimates were within 10% of the actual birth weight compared to 66% for clinical estimates and 42% for sonography.[39] Herrero et al also found that parous women could subjectively estimate the weight of their fetus within 10% of actual weight just as accurately as a physician using abdominal palpation(62% vs. 60.9%) and in their study neither maternal factors such as race, age and parity, nor physician experience improved the fetal weight estimations.[40]

A fourth method of estimating fetal weight was cited by Nahum et al and validated using 3 databases.[41,42,43]. It uses parental and pregnancy-specific information such as maternal height, race, pregnancy weight gain, parity, fetal gender and gestational age to predict birth weight. This technique proved superior in predicting fetal macrosomia with 57% sensitivity, 90% specificity and positive and negative predictive values of 47% and 93% respectively.[41,42]

The medical world is innovative, constantly changing and developing. With the advent of new technologies, estimating fetal weight may eventually become more accurate than previously described. It appears that fetal weight estimates using a 90 second single shot spin-echo sequence MR acquisition with 8-mm thick slices in the axial plane at term are extremely accurate and are better than sonographic estimates. This may be helpful in identifying infants at risk for shoulder dystocia, that occurs with maternal diabetes or post term gestations as well as growth restricted infants, where timing and mode of delivery are affected by fetal weight.[44].

Much debate surrounds the optimal management of a suspected macrosomic infant, where the role of elective caesarean section or induction of labour is questioned. Induction of labour appears to have little benefit to mother or baby, as it may result in an increased caesarean delivery rate without improving perinatal outcomes.[45] A systematic review of current literature by Sanchez-Ramos et al suggests that labour should not be induced in non-diabetic pregnancies, and therefore, expectant management appears to be the accepted policy,[45,46] i.e. await spontaneous labour or induce labour after 42 weeks completion.[10] This rationale may be based on the inaccuracies of prediction of fetal macrosomia.[14]

Caesarean delivery appears to be protective for brachial plexus injury. [1] However, a great number of caesarean section deliveries have to be performed to avoid a

single case of brachial plexus paresis resulting from a difficult shoulder delivery.[10] Rouse and Owen (1999) concluded from their study that mandating prophylactic caesarean delivery at a macrosomia threshold of 4000g by ultrasound in pregnancies not complicated by diabetes would require 2345 caesarean sections and 4.9 million dollars to avert a single brachial plexus injury. With a macrosomia threshold of 4500g, 3695 caesarean deliveries would be need to be performed at a cost of 8.7 million dollars per permanent injury averted, demonstrating the poor performance of such ultrasound policies [1, 30] This evidence appears contrary to the obstetric belief that caesarean section at a greater estimated fetal weight would avert more fetal injury and although in modern obstetrics our management follows evidenced based principles, future research would be needed prior to changing the protocol for performing caesarean sections for large for gestational age babies, especially those >4500g.

Studies suggest that interventions such as caesarean delivery may function more effectively in populations that are at increased risk for macrosomia, i.e. women with diabetes or those who have had prior large infants.[1] The most favourable cost-benefit ratio for elective caesarean section in suspected macrosomic infants was found in diabetic women.[25,30]

With all this information in the background, our study was undertaken with four primary objectives in mind:

1. To determine the prevalence of macrosomic babies delivered at Coronation (now Rahima Moosa) Hospital.
2. To compare the maternal and neonatal outcomes between vaginally born macrosomic babies versus vaginally born babies less than 4000g.
3. To determine maternal and neonatal outcome according to mode of delivery of the macrosomic babies.
4. To compare clinical variables for macrosomia noted in our study with those published in the literature.

3 PATIENTS AND METHODS

Our study took place at Coronation (Rahima Moosa) Hospital, Gauteng, a secondary level hospital and referral centre that serves a population of predominantly low and medium socio-economic status. The study period was from 1 January 2005 – 30 June 2005. Permission to perform this study was obtained from the CEO of Coronation (Rahima Moosa) Hospital after approval was granted by the Human Research Ethics Committee (University of the Witwatersrand).

THERE WERE THREE PARTS TO THIS STUDY:

The **FIRST PART** was a retrospective descriptive study. We included all the viable live births (≥1000g) and all the macrosomic live births, irrespective of mode of delivery, to calculate the prevalence of macrosomia in our study population that were delivered over a 6 month period, 01-01-05 to 31-06-05 at the hospital.

The **SECOND PART** was a retrospective birth cohort, which compared the outcome of vaginally delivered macrosomic babies with babies weighing 2.5-3.99kg who were also **born vaginally**. Maternal and fetal outcomes were compared in these two groups. The control patient (non-macrosomic group) was defined as the subsequent vaginal delivery following the macrosomic delivery in the maternity register, provided it fulfilled the inclusion criteria of our study. The control or non-macrosomic group was matched 1:1 to the macrosomic group.

The **THIRD PART** was a retrospective analysis of the macrosomic infants only and compared maternal and foetal outcomes according to **mode of delivery,** namely **vaginal delivery vs. elective vs. emergency caesarean section.**

We defined fetal macrosomia as a fetal weight ≥ 4000g, the currently accepted definition of the developed world .[15]

Data were obtained from three sources namely, a birth register kept in the labour ward and theatre, maternal case files and antenatal clinic cards.

Data were collected and recorded on a data sheet. Clinical variables used on the data sheet included maternal age, maternal race, parity, gestational age, fetal sex, history of or presence of maternal diabetes or gestational diabetes, previous macrosomic baby and maternal weight gain during pregnancy. Mode of delivery was also noted. Maternal height measurements are not routinely performed at Coronation (Rahima Moosa) hospital and therefore maternal body mass index (BMI) was not included in our data sheet.

Maternal outcomes documented included length of labour, length of second stage, progress on the partogram, use of augmentation, perineal trauma, postpartum haemorrhage, puerperal fever - defined as a temperature rise above 37.8^0C maintained over 24 hours or recurring during the period from the end of the 1^{st} to the end of the 10^{th} day postpartum) and puerperal sepsis - defined as a toxic condition caused by infection in the birth canal, occurring as a complication or sequel of pregnancy.

The fetal outcomes documented included fetal distress, fetal hypoxia defined as deficient oxygenation of fetal blood and expressed as an apgar score <7 at five minutes, apgar scores, presence or absence of shoulder dystocia, any fetal fractures, neurological and or brachial plexus injuries, admission to intensive care unit and admission to the paediatric wards. Admission to neonatal intensive care unit (NICU) occurred in accordance to the paediatric department at Coronations

protocol, which includes admission for respiratory failure, carbon dioxide retention, a drop on arterial and venous ph, meconium aspiration, persistent pulmonary hypertension of the newborn and birth asphyxia (this is dependent on the severity of the asphyxia and the availability of NICU beds.)

Macrosomic infants are routinely observed either in the neonatal ward or with their mothers in the ward for 24 hours and have 4 hourly analysis of serum glucose using the heel prick test.

Postpartum haemorrhage was defined as estimated blood loss greater than 500ml in a normal vaginal delivery and 1000ml in a caesarean section or blood loss causing haemodynamic instability and or requiring blood transfusion. Maternal trauma was defined as follows: A first degree tear was defined as injury to perineal skin only, a second degree tear as an injury to the perineum involving perineal muscles but not involving the anal sphincter. A third degree tear was defined as an injury to the perineum involving the anal sphincter complex and a fourth degree tear involved injury to the perineum involving the anal sphincter complex and anal epithelium.[47]

Babies weighing <2.5kg, multiple pregnancies and stillbirths were excluded from this study. The majority of normal vaginal deliveries at Coronation hospital are performed by nurses/midwives and only complicated deliveries require doctors'

involvement. The majority of caesarean sections performed are by the registrar on duty in theatre or on call.

Data analysis was performed using Epi-info 6 statistical software. Descriptive analysis was used to meet objective 1 i.e. calculation of the prevalence of macrosomia in the study population. Analytic statistics were done using Chi-squared and Fisher's exact test for comparisons of frequencies .Student's t-test and Kruskal Wallis tests were used for comparison of continuous and ordinal data as applicable. A p-value < 0.05 was accepted as indicating statistical significance.

4 RESULTS

4.1 PART 1: PREVALENCE

A total of 134 macrosomic infants were identified in the study period, of which 76 were delivered vaginally, 14 by elective caesarean section and 44 by emergency caesarean section. However 2 of the files of the 76 macrosomic infants delivered vaginally could not be found and data was hence unavailable. These two in fact were removed from the final analysis which therefore included 132 macrosomic infants, 74 of which delivered vaginally, 14 by elective caesarean section and 44 by emergency caesarean. During the study period, there were 5800 deliveries, of which 4636 delivered vaginally and 1164 by caesarean section. The incidence of macrosomia in the study population was 2.3% and the overall caesarean section

rate for all was 20%. Caesarean section for the delivery of macrosomic infants accounted for 5% of the total caesarean section rate.

4.2 PART 2: MACROSOMIC VERSUS NON-MACROSOMIC INFANTS BORN VAGINALLY

This part of the study included data of the 74 macrosomic infants delivered vaginally and was compared to the data of 74 non-macrosomic infants as the control group matched on a 1:1 ratio.

The epidemiologic and obstetrics characteristics of the population are demonstrated in Table 1.

4.2.1 Table 1.Maternal demographics, obstetric and clinical variables for vaginally delivered macrosomic versus non-macrosomic infants.

Variable	Macrosomic (74)	Non-macrosomic (74)	p-value
Maternal race (number)	74	74	0.62
- African	62	60	
- Coloured	7	10	
- Asian	2	3	
- Caucasian	3	1	
Maternal age (years) (±SD)	28.1 (5.7)	27.0 (5.5)	0.24
Parity (number)	74	74	0.96
- 0	19	18	
- 1	25	27	
- 2	18	18	
- 3	8	8	
- 4+	4	3	
Gestational age (weeks) (±SD)	39.0 (1.3)	38.0 (1.3)	<0.0001
Gestational age ≥ 41 weeks (number)	8	1	0.017
Birth weight (grams) (±SD)	4145 (172)	3153 (354)	<0.0001
Male: female ratio (number)	52:22	32:42	0.0009
Partogram (number)	n=60	n=52	0.012
-Normal	49	50	
-Alert	11	1	
-Action	0	1	
Diabetes mellitus (number)	0	0	N/S
Gestational diabetes (number)	0	2	N/S
Previous big baby (number)	8/62	8/48	0.58

SD standard deviation

N/S not significant

Stratifying the patients according to race, showed no significant difference between the macrosomic and non-macrosomic group when analysed using the chi square test p=0.62.

Maternal age ranged from 15 years (2 patients) to 45 years (1 patient). Gestational age ranged from 35-43 weeks gestation. In the macrosomic group the range of birth weights was 4000g-5520g, with a mean weight of 4145g (±172).

In 60 with macrosomic infants and 52 mothers with non-macrosomic infants, a partogram was used or could be extrapolated. The results were: In the macrosomic group, 49/60 had a normal partogram, 11/60 crossed the alert line and 0/60 crossed the action line (p=0.012).

In the non macrosomic group, 50/52 had a normal partogram, 1/52 crossed the alert line and 1/52 crossed the action line.

No patient in either group(macrosomic vs. non macrosomic infant) was a known diabetic, although 2 patients in the non-macrosomic group had gestational diabetes.

Eight (8) patients from each group had previously had macrosomic babies, 8/62 in the macrosomic group and 8/48 in the non-macrosomic group (p=0.58). This was not statistically significant.

Table 2 demonstrates the findings for fetal outcome.

4.2.2 Table 2. Comparison of fetal outcome in the macrosomic vs. non-macrosomic infants that were delivered vaginally.

Variable	Macrosomic (74)	Non-macrosomic (74)	p value
Apgar score (number)			
-Apgar1 <7	3	3	N/S
-Apgar5 <7	0	0	N/S
-Apgar10 <7	1	0	N/S
Shoulder dystocia (number)	5	0	0.03
Fractures(number)	0	0	-
Neonatal ICU admission (number)	0	0	-
Admission to paediatric ward (number)	9	6	0.40

The incidence of fetal distress did not differ in the 2 groups with 2 non-macrosomic and 1 macrosomic babies being described as having fetal distress. This was based on clinical impression only. The incidence of hypoxia was not different between the two groups.

Shoulder dystocia occurred in 5 of the 74 macrosomic and in none of the non-macrosomic babies respectively. This was significantly different in the two groups (p=0.03) No babies suffered fractures at delivery, nor were there admissions to

paediatric ICU. Nine of the 74 macrosomic infants and 6 of the 74 non-macrosomic infants were admitted to the paediatric ward for observations ($p = 0.40$).

Data relating to labour and maternal outcomes after normal vaginal delivery are noted in Table 3.

4.2.3 Table 3. Labour and maternal outcome: macrosomic vs. non-macrosomic, vaginally delivered infants

Variable	Macrosomic (74)	Non-macrosomic (74)	P value
Length of labour (±SD) in hours	13.7 (7.6) n=72	10.9 (5.6) n=73	0.032
Length of second stage (±SD) in minutes	26.7 (24.5)	20.4 (16.0)	0.12
Use of augmentation (number)	16	5	0.009
Perineal trauma(number)	74	74	
- Nil	40	55	-
-1st degree tear	18	9	0.010
-2nd degree tear	1	4	-
-3rd degree tear	0	0	-
- Episiotomy(number)	15	6	0.03
Post partum haemorrhage(number)	10	2	0.016
Puerperal fever (number)	4	1	N/S
Puerperal sepsis (number)	0	0	N/S
Birth weight (grams) (±SD)	4145 (172)	3153(354)	<0.0001

The length of labour in the in the macrosomic group was 13.7 hours (±7.6) and in the non-macrosomic group was 10.9 hours (±5.6) (p=0.032). The length of labour was only calculated or found in 72 of the 74 macrosomic infants and 73 of the 74 non-macrosomic infants. The length of second stage was 26.7 minutes (±24.5) in

the macrosomic group vs.20.4 minutes (±16.0) in the non-macrosomic cohort (p=0.12). Use of augmentation was significant in the macrosomic group where 16/74 patients received augmentation vs. 5/74 of the non-macrosomic group (p=0.009).

When analysing the severity of perineal trauma, there was a significant difference in perineal damage between the macrosomic (34/74) and non-macrosomic (19/74) cohorts (p=0.010). When analysed according to the number of episiotomies performed in each group, a significant difference was found, with 15/74 episiotomies in the macrosomic group vs. 6/74 in the non-macrosomic group (p=0.03). It is not policy at Coronation (Rahima Moosa) Hospital to perform routine episiotomies. An episiotomy is performed selectively according to the doctor or midwife's clinical discretion.

Post partum haemorrhage reached statistical significance with 10/74 cases in the macrosomic group vs. 2/74 in the non macrosomic group. None of these patients required blood transfusions. Puerperal fever occurred more commonly in the macrosomic group i.e. 4 vs. 1, although this did not reach statistical significance.

4.3 PART 3: MODE OF DELIVERY: COMPARISON OF MACROSOMIC INFANTS ACCORDING TO VAGINAL DELIVERY VS. ELECTIVE VS. EMERGENCY CAESAREAN DELIVERY.

A separate analysis was performed comparing epidemiological factors, clinical variables and maternal and fetal outcomes using the 3 different modes of delivery for all the macrosomic fetuses' i.e. normal vaginal delivery, elective and emergency caesarean section. Of the 132 macrosomic infants, 74 were delivered vaginally, 14 by elective caesarean and 44 by emergency caesarean section during the study period. Of the macrosomic babies delivered by caesarean section, 2 were performed for antenatally diagnosed macrosomia –suspected clinically and by ultrasound (the one patient was a gestational diabetic and the other a known insulin dependent diabetic), 2 on maternal request for sterilization in a multiparous patient, 2 for breech presentation, 2 for suspected cephalopelvic disproportion and in 5 patients who had had a previous caesarean section. Twelve of the emergency caesarean deliveries were for fetal distress, 4 in patients who had had a previous caesarean section and had not progressed appropriately in this labour, 23 for cephalopelvic disproportion, 3 for breech presentation in labour, 1 for prolonged rupture of membranes and 1 for macrosomia.

Table 4 illustrates the demographic and epidemiological details for the three different modes of delivery study (macrosomic only) groups.

4.3.1 Table 4. Comparison of the demographic, epidemiological differences and clinical variables in the three different mode of delivery groups for MACROSOMIC infants.

Variable	Vaginal delivery (74)	Elective caesarean (14)	Emergency caesarean (44)	Total (132)	P value
Maternal Race(number)	74	14	44	132	0.167
- *African*	62	9	40	111	
- *Coloured*	7	4	3	14	
- *Asian*	2	1	0	3	
- *Caucasian*	3	0	1	4	
Age (years) (±SD)	28.1 (5.7)	30.6 (7.7)	28.8 (5.6)	28.6 (5.9)	0.33
Parity (number)					0.40
- *0*	19	5	19		
- *1*	25	4	12		
- *2*	18	3	5		
- *3*	8	0	7		
- *4+*	4	2	2		
Gestational age (weeks) (±SD)	39.0 (1.3)	39.1 (1.6)	38.3 (1.9)	39.1 (1.6)	0.28
Birth weight (grams) (±SD)	4145.2 (172)	4161.0 (197)	4246.0 (272)	4180(216)	0.079
Male to female ratio	52:22	10:4	25:20		0.23
Previous big baby (number)	8 (n=62)	4 (n=11)	3 (n=37)		0.055
Diabetes mellitus (number)	0	1	0		0.10
Gestational diabetes (number)	0	1	0		0.10
Partogram (number)	n=60		n=25		0.01
- Normal	49	-	11		
- Alert	11	-	9		
- Action	0	-	5		

The partogram was used in 60 of the patients who had a normal vaginal delivery, and in only 25 of the patients who had emergency caesarean sections. In the normal vaginal delivery group, 49/60 had normal partograms, 11/60 had crossed the alert line and none crossed the action line. In the emergency caesarean section deliveries, 11/25 had normal partograms, 9/25 crossed the alert line and 5/25 crossed the action line ($p=0.01$).

There was only one diabetic and one gestational diabetic in this section of our study group, both of whom were delivered by elective caesarean section.

A significant number of the babies delivered by emergency caesarean section had foetal distress ($p=0.0001$). See Table 5 which shows outcome measures of neonates according to mode of delivery.

The one minute apgar score shows that a total of 3 neonates born by normal vaginal delivery had apgar scores of <7 vs. 0 in the elective caesarean delivery group and 1 for the emergency caesarean group. This was not significant.

Data comparing differences in fetal outcome for the three groups is illustrated in Table 5.

4.3.2 Table 5. Comparison of fetal outcome in the macrosomic group of neonates stratified according to mode of delivery.

Variable	Vaginal delivery	Elective caesarean	Emergency caesarean	p value
Fetal distress(number)	1	0	13	<0.0001
Hypoxia(number)	2	0	4	N/S
Fractures(number)	0	0	0	-
Admission to ICU (number)	0	0	0	-
Admission to paediatric ward (number)	9	0	2	0.17
Apgar score (number)				
- Apgar1 <7	3	0	1	0.16
- Apgar5 <7	0	0	0	-
- Apgar10 <7	1	0	0	N/S

Data comparing differences in labour and maternal outcomes for the three groups is illustrated in Table 6.

4.3.3 Table 6. Outcome of mothers with macrosomic infants stratified according to mode of delivery

Variable	Vaginal delivery	Elective caesarean	Emergency caesarean	p value
Use of augmentation (number)	16	0	12	0.48
Post partum haemorrhage (number)	10	0	4	
Puerperal fever (number)	4	5	14	0.0001
Puerperal sepsis (number)	0	0	1	N/S

Augmentation was given to 21.6% of the patients in the vaginal delivery group vs. 27.3% of the emergency caesarean section group which was not significantly different.

Ten of the 74 patients in the vaginal delivery group, none of the elective caesarean deliveries and 4 of the 44 patients having emergency caesarean deliveries had post partum haemorrhage. A significant number of patients who had elective and emergency caesarean section developed puerperal fever, 36% and 32% respectively vs. 5% of vaginal delivery, (p=0.0001) and 1 patient from the emergency caesarean group suffered from puerperal sepsis, which was not significant.

5 DISCUSSION

Interestingly, the incidence of macrosomia in our study group was only 2.3%. As described earlier, the incidence of macrosomia in different countries is extremely variable, and the lower incidence in our study is somewhat similar to that expressed by others, namely 3.43%at the Umtata Hospital in the Eastern Cape[15] , 3.4% at the Kuopio University Hospital, Finland[22] and 2.3% at the Chiawelo Clinic Soweto[16] respectively.[15,16,22] The low incidence in our study, and those mentioned above are in sharp contrast to the greater incidence seen in the United States, where macrosomia complicates more than 10% of all pregnancies[12,48] and in Denmark and the Republic of Croatia where it has surprisingly been shown to be ≥ 20%.[14] As was theorized earlier the possible explanation for this may be the alarming increase in obesity in the affluent countries. [19] In Scotland alone the number of women with a body mass index above 30(clinically obese) has doubled with 9.4% defined as obese in 1990 vs. 18.9% in 2002/2004.[20]. This has been followed by a rise in the prevalence of type 2 diabetes in these developed countries. In Germany the prevalence of overweight and obesity has increased significantly from 1991-1998 and the prevalence of type 2 diabetes increased 20-fold over the last 50 years, resulting in 4.6% of the population now being afflicted.[19].

Several risk factors for the development of fetal macrosomia have been identified, namely advancing maternal age, ethnicity (Caucasian)[17] , high parity, height or

stature, weight gain during pregnancy, maternal obesity (BMI>30)[18], previous history of macrosomic infant, impaired glucose tolerance, maternal diabetes, prolonged pregnancy (>40 weeks gestation)[17], non smokers and male fetus. Unfortunately, maternal weight, weight gain during the pregnancy and height are not recorded on the antenatal clinic cards at Coronation (Rahima Moosa) Hospital and therefore this data was not available for analysis.

In our study, the mean maternal age in the macrosomic group was 28.1 years (±5.7) versus 27.0 years (±5.5) in the non-macrosomic group. This difference was not found to be significant, although there was a trend towards mothers with macrosomic infants having a more advanced maternal age, i.e. a mean of 28.6 years (±5.9). Of interest to note is that the mean maternal age in the elective caesarean group was 30.6 years (±7.7). These findings are similar to those of larger studies that suggest that older women (in their third decade or more) are at an increased risk of having a macrosomic infant. [11,13,15,48] Stotland el al (2004) found that a maternal age of 30-40 years was associated with macrosomia, [11] and Jolly et al (2003) found fetal macrosomia was more likely to occur in women who were >40 years of age (Odds ratio 1.22, Confidence interval 1.11, 1.35). [13]

With regards to maternal race/ ethnicity, analysis of our data revealed no statistical significance (p=0.62), with similar values for each race in both the study and control cohorts and when comparing mode of delivery. Incidentally there was only

a small number of Caucasian patients in our study, 5 in total. This may possibly be the reason for the reduced incidence of macrosomia in our study population as seen in other studies [15,16] as Caucasian race appears to be a significant risk factor for macrosomia in several studies.[11,13,48.] The number of Caucasian patients delivering at Coronation (Rahima Moosa) Hospital is small compared to non-Caucasian patients. All patients at Coronation (Rahima Moosa) are screened for gestational diabetes if their risk profile according to their by history or antenatal findings deems it necessary, i.e. previous gestational diabetes, family history of diabetes, previous macrosomic infant, previous unexplained intrauterine fetal death or congenital abnormality, maternal weight >100kg and persistent glycosuria. Routine screening is not undertaken.

Increased maternal parity appears to be associated with fetal macrosomia.[49] This sentiment was echoed by Jolly et al (2003) in their study, where women with a parity of >4 were found to be more likely to deliver macrosomic infants (OR 2.20, CI 2.02, 2.40).[13] Mulik et al (2003) in their study looked at the outcome of macrosomic fetuses in a low risk primigravid population. It was interesting to note that the incidence of macrosomia in their study population was 9 %.[48] In our study, parity was not a significant factor when considering the macrosomic vs. non-macrosomic babies (p=0.96) or when considering mode of delivery of the macrosomic infants (p=0.40). A cohort study of 146 526 mother-infant pairs by Stotland et al (2004) concluded that multiparity was a predictor of macrosomia.[11] We can not draw the same conclusion from our study. A total of 15 patients from

the macrosomic group had previously had macrosomic infants and 8/48 from the non-macrosomic group had previously had macrosomic infants, although this difference was not significant (p=0.58). Although not found in our study, prior studies have shown that previous history of a macrosomic birth was an independent risk factor of fetal macrosomia.[15,22]

Gestational diabetes and maternal diabetes appeared not to be common findings in our study population (present in only 2 patients in the macrosomic group elective caesarean group and 2 in the non-macrosomic group). This is in contrast to the literature, which strongly links gestational diabetes [15,50] and maternal diabetes [11] to macrosomia.[13,22] In fact, Zamorski et al (2001) felt that the strongest risk factor for macrosomia is maternal diabetes, which results in a twofold increase in the incidence of macrosomia.[12] Daponte et al in their review of management in a diabetic pregnant patient found that almost one third of babies born to a diabetic mother was macrosomic. [51] Interestingly almost double the number of macrosomic babies occurred in moderately controlled patients as compared to well or strictly controlled patients. [51] Adams et al (1998) suggest that unrecognized gestational diabetes increases the risk of large for gestational infants, macrosomia, shoulder dystocia and birth trauma, independent of maternal obesity and other confounding variables.[52] Unrecognized gestational diabetes is a possible reason for the reduced incidence of impaired glucose tolerance in our study population, whilst ethnicity could be another. In our study we found that both of the diabetic patients in the macrosomic group – one in a mother who had gestational diabetes and the

other a known insulin dependent diabetic were delivered electively by caesarean section after discovery of macrosomic features on ultrasound.

Prolonged pregnancy (gestational age >41 weeks) [11] and postdatism (>42 weeks of gestation) [15, 22] have all been identified as independent risk factors for macrosomia. The findings in our study are congruent with those of previous reviews with the study group having a significantly more advanced gestational age 39.0 weeks (±1.3) vs. 38.0 weeks (±1.3) than the control group ($p<0.0001$).The average gestational age of all the macrosomic infants was 39.1 weeks (±1.6). Eight (8) times the number of infants in the macrosomic group had a gestational of ≥ 41 weeks when compared to the non macrosomic group i.e. 11% vs.1.3%. $p=0.017$.

The preponderance of male infants in our study is in agreement with findings from other studies.[11,15,22] In our study, over 70% of the macrosomic infants were male vs.43% in the control group ($p=0.0009$). These findings follow through into the macrosomic, mode of delivery part of the study where 66% of these infants were male. It is evident from the literature that there are a multitude of risk factors associated with the possible development of macrosomia. Yet, Zamorski et al (2001) who analyzed this concept, found that only 32% of infants developed macrosomia when two or more risk factors were present, 34% of macrosomic

babies were born to mothers without any risk factors, and 38% of pregnant women have at least one risk factor.[12]

6 MATERNAL OUTCOMES

Macrosomia has been associated with several adverse maternal outcomes, namely; increased risk for delivery by caesarean section, [12] increased perineal tears and trauma, [11] obstructed labour, post partum haemorrhage, prolonged labour, increased use of augmentation [11,13,48] risk of instrumental vaginal delivery, [13] prolonged hospital stay and chorioamnionitis.[11]

In the normal vaginal delivery component of our study, our findings concurred with the literature in terms of the increased incidence of post partum haemorrhage, (10 vs. 2), increased incidence of third degree tears and severe perineal trauma,(15 vs. 6) and puerperal fever (4 v 1), amongst the mothers that delivered macrosomic babies versus those mothers that delivered non-macrosomic babies, all of which were statistically significant. Also of note was the increased need for augmentation in the macrosomic group (16 v 5) which suggests an underlying dysfunctional labour (p=0.009). This may also explain the prolonged length of labour in the macrosomic group (13.7 hours (±7.6) vs. 10.9 hours (±5.6) (p=0.032) and increased length of second stage. (26.7 minutes (±24.5) vs. 20.4 minutes (±16.0) (p=0.12).

Xenakis et al (1997) discovered that any oxytocin requirement in labour is associated with a greater increase in caesarean section rate for macrosomic than for non macrosomic pregnancies.[53] This is confirmed in our study by the fact that 12/44 (27%) of the macrosomic infants delivered by emergency caesarean section had received augmentation before proceeding to caesarean section. It may be that cephalopelvic or feto-pelvic disproportion with ineffective uterine action due to the increased uterine volume may have been the underlying cause for the prolonged or dysfunctional labour requiring augmentation. These deductions are implied by the fact that 20% of the patients requiring delivery by emergency caesarean section had crossed the action lines on the partogram. The majority of deliveries by emergency caesarean, 23/44 (52%) were performed for cephalopelvic disproportion, (which included deliveries by emergency caesarean section for poor or no progress), these findings concur with those in the literature.

Higher rates of serious intra- and postoperative maternal complications have been reported for delivery by caesarean section as compared to vaginal delivery.[25,54] Puerperal fever, sepsis and post partum haemorrhage are some of the maternal complications cited in the literature.[10, 55] In our study 10 (13.5%) of the women who had normal vaginal deliveries suffered post partum haemorrhage compared to 4 (9%) in the emergency caesarean section group and none in the elective caesarean section group. Conway et al (2002) found more complications in women delivering macrosomic infants vaginally than in women delivering macrosomic infants by caesarean section without labour.[3, 54] Our findings concur

with their studies. Results from our study differ slightly from the literary findings in terms of poorer outcomes with caesarean section, when comparing vaginal deliveries with emergency caesarean section. However the better outcome of elective vs. emergency caesarean section, in terms of post partum haemorrhage, supports literary findings that the complication rates of unplanned operations are higher than planned operations. [55]

Regarding other complications such as puerperal fever and sepsis, our findings concurred with the literature as 5 (36%) patients in the elective caesarean section group, 14 (32%) in the emergency caesarean section group and only 4 (5%) in the normal vaginal delivery group experienced puerperal fever (p=0.0001). The increased incidence among women who had an elective caesarean section may be misleading however, due to the small number of patients in this group. The increased incidence of puerperal fever among women who had an emergency caesarean vs. normal vaginal delivery group however, was statistically significant. One patient from the emergency caesarean section group suffered from puerperal sepsis.

7 FETAL OUTCOMES

Low apgar scores, [13] fetal distress, fetal hypoxia, [12] paediatric ICU admission, [56] admission to paediatric wards, [13] shoulder dystocia, [12, 57] brachial plexus and

neurological injuries as well as clavicular and humeral fractures are among the fetal complications and adverse fetal outcomes associated with fetal macrosomia.[25, 48] Herbst (2005) found that neonatal fractures of the clavicle and/or humerus occur in 1-2% of vaginal deliveries, with an increased incidence that is associated with shoulder dystocia.[46] Of interest, in our study, there were no clavicular or humeral fractures.

In the macrosomic versus non macrosomic part of our study, each group had equal numbers of babies with an apgar score <7 at one minute i.e. 3 and the macrosomic group had 1 baby with an Apgar score <7 at 10 minutes. These findings were not statistically significant.

Haram et al (2002) found that Apgar scores were often lower in macrosomic babies delivered by caesarean section compared with vaginal deliveries.[10] Our findings, with regards to apgar scores, did not confirm this, nor did they reach statistical significance, with 4 babies from the normal vaginal delivery group and 1 from the emergency caesarean section group having apgar score of <7 at one, five or ten minutes (p=0.16).

Fortunately none of the neonates in our study required a neonatal intensive care unit (NICU) admission. Gillean et al (2005) in a study analysing admission of macrosomic infants to neonatal intensive care unit identified risk factors for prolonged NICU stay. Among other factors, they found that prolonged labour per

se did not put the fetus at risk, but rather the consequences of prolonged labour such as fever, caesarean section delivery and low apgar score.[56] These findings indicate that macrosomic infants warrant increased attention in labour.[56,59] Of interest was that diabetes, caesarean section delivery and lower gestational age doubled the risk of admission.[56] Their findings are similar to those of Nasser et al (2003) who found longer nursery stays among neonates born by caesarean section. [56,60] Haram et al (2002), noted that there is a lower reported incidence of the use of neonatal intensive care after vaginal delivery (2.1%) compared with caesarean section (6.0%).[10]

In our study, although not statistically significant, 9 macrosomic infants vs. 6 non macrosomic infants required admission to the paediatric ward for observation (p=0.40). Macrosomic infants delivered vaginally were three times more likely to require observation in the paediatric ward than infants born by elective caesarean section (12% vs. 4.5%). Differences in the findings of fetal distress and hypoxia in the macrosomic and non-macrosomic group did not reach statistical significance; similar results were found in the mode of delivery group regarding hypoxia. However, a significant number (29.5%) of babies in the emergency caesarean delivery were reported to have fetal distress ($p<0.0001$).

Shoulder dystocia is marked by difficulty in delivery of the anterior fetal shoulder after the appearance of the fetal head on the maternal perineum. Acker et al (1985) first described the details of this association.[1] They found the incidence of shoulder dystocia in their population to be 0.2% in infants weighing 2500-2999g,

0.6% for 3000-3499g, 2.2% for 3500-3999g, 10% for 4000-4499g and 22.6% for infants weighing more than 4500g.[1] The shoulder dystocia rate among macrosomic infants born vaginally is significantly higher than among appropriately grown infants, and the rate among diabetic women is higher than among non-diabetics. Langer et al (2000) found a shoulder dystocia rate of 0.3% when birth weight was <4000g and 4.9% when ≥ 4000g. Non diabetic women had an overall shoulder dystocia rate of 0.5% compared to 3.2% in diabetic women.[25,54] In our study none of the patients from the non-macrosomic group (<4000g) had shoulder dystocia versus 6.8% or 5/74 from the macrosomic group and none of these patients were diabetic. None of the patients delivered by caesarean section suffered shoulder dystocia, or its complications. “Increased birth weight is a well described risk for brachial plexus injury. As expected, the incidence of brachial plexus injury increases with increasing birth weight. Among infants born to non-diabetic mothers, the incidence was 0.5 out of 1000 live births among infants weighing less than 4000g compared with 26.8 out of 1000 live births for infants weighing more than 5000g.”[1] Fortunately none of the neonates in either part of our study suffered from brachial plexus injuries. Ecker et al (2004) found that the presence of pregestational or gestational diabetes was associated with increased risk for brachial plexus injury (odds ratio=3.19).[1] The low incidence of pregestational or gestational diabetes in our study population may provide a partial explanation for the absence of brachial plexus injuries in our study.

The fact that the adverse maternal and fetal outcomes in the macrosomic and mode of delivery component of our study differ so slightly and that macrosomic infants born vaginally appear to do well, with few adverse sequelae, leads one to deduce that elective caesarean section for suspected macrosomia may result in a high number of unnecessary surgical procedures. Early induction of labour to limit fetal growth, may result in a substantial increase in the caesarean section rate because of failed inductions.[12] Expectant management of the suspected macrosomic infant appears appropriate.[45,46]

The ACOG practise bulletin no. 22 provides similar recommendations:[26]

1. Based on good and consistent scientific evidence:
    a. The diagnosis of fetal macrosomia is imprecise and the accuracy of estimated fetal weight using ultrasound biometry is no better than that obtained with clinical palpation.
2. Based on limited or inconsistent scientific evidence:
    a. Suspected fetal macrosomia is not an indication for induction of labour, because induction does not improve maternal or fetal outcome.
    b. Labour and vaginal delivery are not contraindicated for women with estimated fetal weights up to 5000g in the absence of maternal diabetes.

c. With an estimated fetal weight of more than 4500g, a prolonged second stage of labour or arrest of descent in the second stage is an indication for caesarean delivery.

3. Recommendations based primarily on consensus and expert opinion:

   a. Although the diagnosis of fetal macrosomia is imprecise, prophylactic caesarean delivery may be considered for suspected fetal macrosomia with estimated fetal weights of more than 5000g in pregnant women without diabetes and more than 4500g in pregnant women with diabetes.

   b. Suspected fetal macrosomia is not a contraindication to attempted vaginal birth after a previous caesarean delivery.[26]

8 LIMITATIONS

There are a number of limitations to our analysis and data collection. Several of the maternal files were incomplete. The information we obtained from the maternal antenatal clinic cards, maternal files and maternity register did not include maternal weight, height or maternal pregnancy weight gain, which, in the literature, have been shown to be important risk factors for fetal macrosomia. Our study was also limited by the fact that we do not have long term follow up of both the mothers and their macrosomic infants, to assess the long term consequences associated with macrosomia. Another limitation is the small sample size; a larger study population could provide more substantial analyses.

9 RECOMMENDATIONS

From the published literature and data obtained from our study, the following concepts appear most significant:

During the antenatal period, a high index of suspicion is vital and careful follow up at an antenatal clinic is recommended. Risk factors or co-variables may be used as a guide, along with clinical examination and available technology such as ultrasound. As a previous macrosomic baby is a strong predictor of a future macrosomic baby, a detailed obstetric history should be obtained.

Having said this however, it is a well accepted fact that fetal macrosomia is extremely difficult to accurately diagnose predelivery. Nevertheless risk factors should be born in mind when assessing any pregnant woman intrapartum. Assessment may include clinical estimation of fetal weight and sonographic estimation.

Even though this was a small study, and there were only 14 patients that were delivered by elective caesarean section, with respect to the appropriate mode of delivery in the case of fetal macrosomia**,** expectant management of the mother with a suspected macrosomic baby offers an option that is apparently safe, acceptable and comparable to elective caesarean section.

Women in labour require meticulous monitoring with impeccable use of the partogram. Good progress in labour for a suspected macrosomic infant is a reassuring sign. Slow progress of labour, use of augmentation and prolonged second stage should alert the attending physician to the possibility of fetal macrosomia.

As shoulder dystocia is one of the most feared complications of macrosomia, and it is an obstetric emergency, all staff working in labour ward should be adequately trained in the management of this emergency. Regular refresher courses and drills would benefit all in the long run.

More research is needed on the relationship between maternal weight, height, maternal pregnancy weight gain, nutrition, obesity, smoking and the short and long term maternal morbidities associated with fetal macrosomia from a South African perspective. Cost effective management of a suspected macrosomic especially in the developing world may provide some useful management protocols.

REFERENCES

1. Ecker JL. Caesarean delivery for suspected macrosomia: Inefficient at best. Clin Obstet Gynecol 2004;47:352-364.

2. Rosati P, Exacoustos C, Caruso A, Mancuso S. Ultrasound diagnosis of fetal macrosomia. Ultrasound Obstet Gynecol 1992;2:23-29.

3. Barth WH. Fetal Macrosomia. Clinical management. Guidelines for Obstetricians- Gynaecologists. American College of Obstetrician and Gynaecologists. November 2000 Practise Bulletin no. 22.

4. Langer O. Fetal macrosomia: Etiologic factors. Clin Obstet Gynecol 2000; 43:283-297.

5. Vorherr H. Factors influencing fetal growth. Am J Obstet Gynecol. 1982 Mar 1;142(5):577-88.

6. Hill DJ, Petrik J, Arany E. Growth factors and the regulation of growth. Diabetes Care 1998 Aug;21 Suppl 2:B60-9.

7. Nasrat H, Abalkhail B, Fageeh W. Anthropometric measurements of newborns of gestational diabetic mothers: Does it indicate disproportionate growth? J Matern Fetal Med 1997;6:291-295.

8. McFarland MB, Trylovich CG, Langer O. Anthropometric differences in macrosomic infants of diabetic and nondiabetic mothers. J Matern Fetal Med 1998;7:292-295

9. James DK, Steer PJ, Weiner CP, Gonik B. High risk pregnancy Management Options. Third edition, Chapter 12 p261.

10. Haram K, Pirhonen J, Bergsjo P. Suspected big baby: a difficult clinical problem in obstetrics. Acta Obstet Gynecol Scand 2002;81:185-194.

11. Stotland NE, Caughey AB, Breed EM, Escobar GJ. Risk factors and obstetric complications associated with macrosomia. Int J Gynecol Obstet 2004;87:220-226.

12. Zamorski MA, Biggs WS. Management of suspected fetal macrosomia. Am Fam Physician 2001;63:302-306.

13. Jolly MC, Sebire NJ, Harris JP, Regan L, Robinson S. Risk factors for macrosomia and its clinical consequences: a study of 350, 311 pregnancies. Eur J Obstet Gynecol Reprod Biol 2003;111:9-14.

14. Chauhan SP, Grobman WA, Gherman RA, Chauhan VB, Chang G, Magann EF, et al. Suspicion and treatment of the macrosomic fetus: a review. Am J Obstet Gynecol 2005;193:332-46.

15. Essel JK, Opai- Tetteh ET. Macrosomia-maternal and fetal risk factors. S Afr Med J 1995;85:43-46.

16. Buchmann EJ. Perinatal Health in the Chiawelo district of Soweto. Maternal characteristics and clinical outcomes. CHASA J Compr Health 1996;7:118-123.

17. Wallace S, McEwan A. Fetal macrosomia. Obstetrics, Gynaecology and Reproductive Medicine 2007;17:2:58-61.

18. Clausen T, Burski TK, Oyen N, Godang K, Bollerslev J, Henriksen T. Maternal anthropometric and metabolic factors in the first half of pregnancy and risk of neonatal macrosomia in term pregnancies. A prospective study. Eur J Endo 2005;153: 887-894.

19. Bergmann RL, Richter R, Bergmann KE, Plagemann A, Brauer M, Dudenhausen JW. Secular trends in neonatal macrosomia in Berlin: influences of potential determinants. Paediatric and Perinatal Epidemiology 2003; 17:244-249.

20. Fraser RB. Obesity complicating pregnancy. Curr Obstet Gynecol 2006;16:295-298.

21. Ramos GA, Caughey MD. The interrelationship between ethnicity and obesity on obstetrics outcomes. Am J Obstet Gynecol 2005 ;193 :1089-93.

22. Heiskanen N, Raaitkainen K, Heinonen S. Fetal macrosomia – a continuing obstetric challenge. Biol Neonate. 2006;90:98-103.

23. Gonen R, Spiegel D, Abend M. Is macrosomia predictable, and are shoulder dystocia and birth trauma preventable? Obstet Gynecol 1996;88:526-529.

24. Barker DJP. Maternal nutrition, Fetal Nutrition, and Disease in Later Life. Nutrition. 1997;807.

25. Conway DL. Delivery of the macrosomic infant: Caesarean section versus vaginal delivery. Semin Perinatol 2002;26:225-231.

26. American College of Obstetricians and Gynaecologists. Fetal macrosomia. Practise bulletin No. 22 Washington DC: ACOG 2000.

27. Nahum GG. Predicting fetal weight. Are Leopold's Maneuvers still worth teaching to Medical Students and House Staff? J Reprod Med 2002; 47:271-278

28. Shepard MJ, Richards VA, Berkowitz RL, Warsof SL, Hobbins JC. An evaluation of two equations for predicting fetal weight by ultrasound. Am J Obstet Gynecol 1982;142(1):47-54.

29. Nahum GG. Accurate prediction of fetal macrosomia using combination methods. Am J Obstet Gynecol 2006 ;195(3):879-880.

30. Rouse DJ, Owen J. Prophylactic caesarean delivery for fetal macrosomia diagnosed by means of ultrasonography: A Faustian bargain? Am J Obstet Gynecol 1999;181:332-8.

31. O'Reilly-Green C, Divon M. Sonographic and clinical methods in the diagnosis of macrosomia. Clin Obstet Gynecol 2000;43:309-320.

32. Chauhan SP, Hendrix NW, Magann EF, Morrison JC, Kenney SP, Devoe LD. Limitations of Clinical and Sonographic Estimates of Birth Weight: Experience with 1034 Parturients. Obstet Gynecol 1998;91:72-7.

33. Hendrix NW, Grady CS, Chauhan SP. Clinical vs. Sonographic Estimate of Birth Weight in Term Parturients. A Randomized Clinical Trial. J Reprod Med 2000; 45:317-322.

34. Hart NC, Siemer J, Meurer B, Schrauder M, Goeke TW, Beckmann MW, Schild RL. Weight estimation in fetal macrosomia. Ultrasound in Obstet and Gynecol 2006;28:470.

35. Schild RL, Fimmers R, Hansmann M. Fetal weight estimation by three-dimensional ultrasound. Ultrasound Obstet Gynecol 2000;16:445-452.

36. Siemer J, Wolf T, Hart N, Schrauder M, Meurer B, Goeke T, Beckmann MW, Schild RL. Increased accuracy of Fetal Weight Estimation with a Gender Specific Formula. Fetal Diagn Ther 2008; 24:321-326.

37. Hackmon R, Bornstein E, Ferber A, Horani J, O'Reilly Green CP, Divon MY. Combined analysis with amniotic fluid index and estimated fetal weight for prediction of severe macrosomia at birth. Am J Obstet Gynecol 2007;196:333e1-333e4.

38. Hackmon R, LeScale KB, Ferber A, Divon MY. Can severe macrosomia be detected at the time of nuchal translucency screening? Ultrasound Obstet Gynecol 2005; 26:388.

39. Chauhan SP, Lutton PM, Bailey KJ, Guerrieri JP Morrison JC. Intrapartum Clinical, Sonographic, and Parous Patients' Estimates of Newborn Birth Weight. Obstet Gynecol 1992;79:956-8.

40. Herrero RL, Fitzsimmons J. Estimated fetal weight, Maternal vs. Physician Estimate. J Reprod Medicine 1999; 44: 674-678.

41. Nahum GG, Stanislaw H, Huffaker BJ. Accurate prediction of term birth weight from prospectively measurable maternal characteristics. J Reprod Med 1999;44:705-12.

42. Nahum GG, Stanislaw H. Validation of a birth weight prediction equation based on maternal characteristics. J Reprod Med 2002;47:752-60.

43. Nahum GG, Pham KQ, Stanislaw H. Prediction of term birth weight in Hispanic women using an equation based on maternal characteristics. Eur J Obstet Gynecol Reprod Biol 2004; 112:145-50.

44. Hassibi S, Farhataziz N, Zaretsky M, McIntire D, Twickler DM. Optimization of Fetal Weight Estimates using MRI: Comparison of Acquisitions. AJR 2004;183:487-492.

45. Sanchez-Ramos L, Bernstein S, Kaunitz AM. Expectant management versus labor induction for suspected fetal macrosomia: a systematic review. Obstet Gynecol 2002;100:997-1002.

46. Herbst MA. Treatment of suspected fetal macrosomia: A cost effectiveness analysis. Am J Obstet Gynecol 2005;193:1035-9.

47. Royal College of Obstetricians and Gynaecologists. Methods and Materials used in perineal repair. Guideline 23. Revised June 2004.

48. Mulik V, Usha Kiran TS, Bethal J, Bhal PS. The outcome of macrosomic fetuses in a low risk primigravid population. Int J Gynecol Obstet 2003;80: 15-22.

49. Aliyu MH, Jolly PE, Ehiri JE, Salihu HM. High parity and adverse birth outcomes: exploring the maze. Birth 2005;32:45-59.

50. Hyer SL, Shebata HA.Gestational diabetes mellitus. Curr Obstet Gynecol 2005;15:378-374.

51. Daponte A, Guidozzi F, Moisuc D, Marineanu A. Management of diabetic pregnant patients in a tertiary centre in the developing world. Int J Gynecol Obstet 1999; 64:141-6.

52. Adams KM, Li H, Nelson RL, Ogburn PL Jr, Danilenko-Dixon DR. Sequelae of unrecognised gestational diabetes. Am J Obstet Gynecol 1998;178(6):1321-32.

53. Xenikas E M-J, Piper J, Langer O. Likelihood of vaginal delivery in pregnancies complicated by macrosomia. Am J Obstet Gynecol 1997;176 S114.

54. Conway DL, Langer O. Elective delivery of infants with macrosomia in diabetic women: reduced shoulder dystocia versus increased caesarean deliveries. Am J Obstet Gynecol 1998;178(5):922-5.

55. Hager RME, Daltveit AK, Hofoss D, Nilsen ST, Kolaas T, Oian P, Henriksen T. Complications of caesarean deliveries: Rates and risk factors. Am J Obstet Gynecol 2004;190:428-34.

56. Gillean JR, Coonrad DV, Russ R. Big infants in the neonatal intensive care unit. Am J Obstet Gynecol 2005;192:1948-53.

57. Xenikas E M-J, Piper J. Macrosomia: Is vaginal delivery contraindicated? Am J Obstet Gynecol 1997;176(1):S115.

58. Coomarasamy A, Connock M, Thornton J, Khan KS. Accuracy of ultrasound biometry in the prediction of macrosomia: a systematic quantitative review. Br J Obstet Gynaecol. 2005;112:1461-1466.

59. Gregory KD, Henry OA, Ramicone E, Chan LS, Platt LD. Maternal and infant complications in high and normal weight infants by method of delivery. Obstet Gynecol 1998;92:507-513.

60. Nassar AH, Usta AM, Khalil AM, Melhem TI, Nakad TI, Abu Musa AA. Fetal macrosomia (>4500g):perinatal outcome of 231 cases according to the mode of delivery. J Perinatol. 2003; 23:136-141.

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ANNEXURE B: ETHICS CLEARANCE CERTIFICATE

9.1.1 Table 7. Ethics Clearance Certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Toweel

CLEARANCE CERTIFICATE	**PROTOCOL NUMBER M051012**
PROJECT	Fetal Macrosomia Risk Factors and Maternal and Perinatal Outcome Associated with Mode of Delivery
INVESTIGATORS	Dr GD Toweel
DEPARTMENT	Obstetrics & Gynaecology
DATE CONSIDERED	05.10.28
DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 05.09.31 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable

cc: Supervisor : Dr N Pirani

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10005, 10th Floor, Senate House, University.

I/(We) fully understand the conditions under which I am/(we) are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/(we) undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES