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**Sonographic prediction of fetal macrosomia: effect on the mode of delivery  
and value of combined methods to improve fetal weight estimation**

**INAUGURAL - DISSERTATION**  
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## **Table of contents**

## **Page**

1. Summary	2
2. Introduction	4
3. Patients and methods	6
4. Results	9
5. Discussion	21
6. References	25
7. Acknowledgement	30
8. Curriculum vitae	31

## 1. Summary

**Background.** The incidence of fetal macrosomia (infant birth weight  $\geq 4000\text{g}$ ) has been increasing during recent decades and is associated with maternal and fetal complications. Accurate prenatal prediction of macrosomia therefore would be very useful for planning the strategy for delivery. Unfortunately, the accuracy level of birth weight estimation even by modern ultrasound equipment is still relatively low. It may cause potential harm when macrosomia is missed. On the other hand it may increase the number of unnecessary interventions when it is wrongly suspected. A vast variety of investigators have been trying to combine additional clinical and maternal data, considered as risk factors, in the hope for a better estimation of fetal macrosomia. None of these methods has been useful in the routine clinical practice.

**Objective.** This study was conducted to find out, whether the sonographic assessment of the fetal weight at term or near term has had influence on the mode of delivery. Concomitantly, the predictive quality of the recently suggested combined diagnostic methods has been analyzed in comparison to sonographic weight estimation alone in an unselected population.

**Methods.** In the first part of the study 3435 pregnant women, who delivered term, singleton, live born infants between 2004 – 2007 at the University Hospital of Zurich were analyzed. The study population was divided into 4 groups (true positive, true negative, false positive, false negative) according to the estimated fetal weight (EFW) and regarding the birth weight (BW).

In the second part of the study the retrospective cohort data was obtained from 1062 pregnancies of an unselected population. The estimated fetal sonographic weight was obtained within the last week prior to delivery. The combination models published by Mazouni et al. and Nahum and Stanislaw were employed to predict the presence of macrosomia at birth in these infants. Receiver-operating characteristics (ROC) curves were generated to compare the prediction of macrosomia when using different observation methods. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were calculated. The mean values of two groups were compared using two sample t test and  $X^2$  test for comparison of proportions. Additionally,  $X^2$  test was completed by Post Hoc Cell analysis with the Wilson test.

**Results.** The first study population included 364 (10.6%) macrosomic infants within a mean BW of  $3404 \pm 471\text{g}$  and a mean of EFW  $3279 \pm 475\text{g}$ . Cesarean sections were performed for

58.2% of the pregnant women, where fetal macrosomia was truly ruled in (true positive) and for 34.6% of the women who delivered normal weight infants (true negative). Overestimation of fetal weight (false positive) has led to the 46.3% rate of cesarean sections. However, only 27.0% of false negative defined infants were delivered during caesarean section where fetal weight was underestimated. The difference of the cesarean section rate between true positive and false negative groups was equal 0.31 (CI 95%, 0.21 - 0.4) and greater than that between false positive and true negative groups 0.12 (CI 95% 0.01 - 0.23) ( $P < 0.0001$ ).

In the second study population macrosomia was present in 135 of 1062 (12.7%) newborns.

The prediction of a probable macrosomia using ROC curve analysis revealed ultrasound alone to be significantly superior to the Mazouni et al. combined method (AUC 0.922 (CI 95%, 0.902-0.943) vs. 0.747 (CI 95%, 0.700-0.794), ( $P < 0.0001$ ), respectively, whereas the Nahum and Stanislaw equations were similar but not superior to ultrasound alone (AUC 0.895 (CI 95% 0.839-0.950) [3], (AUC 0.887 (CI 95% 0.834-0.941) [4], (AUC 0.885 (CI 95% 0.831-0.940) [11], vs. 0.912 (CI 95% 0.867-0.958) respectively, ( $P < 0.0001$ ).

The accuracy of macrosomia prediction was similar for ultrasound alone and the Nahum and Stanislaw equations (~ 90%) whereas the Mazouni et al. nomogram reached only 51.7% (probability cut-off level of 50%).

**Interpretation.** This study proves the hypothesis that an inappropriate prediction of the fetal weight influences the method of delivery. Underestimation of the fetal weight in the group of macrosomic infants has led to a lesser amount of cesarean sections in comparison with the group where fetal macrosomia was correctly diagnosed. On the other hand, unexpected fetal and maternal complications could occur because of inadequate care during labor. Furthermore, parents would have had a lack of appropriate information and could not participate in taking a decision regarding the mode of delivery.

When applying the model proposed by Mazouni et al. to our unselected population, accuracy of the prediction of macrosomia was distinctly lower than that of ultrasound alone. The best equations of Nahum and Stanislaw for the prediction of macrosomia did not appear to be superior to the ultrasound estimation alone neither. It is true that the error associated with the sonographic estimations of the fetal weight at term reduces its value; nevertheless, currently sonography is still the best and most objective method for birth weight estimation available and a combination with pregnancy specific data does not improve the predictive quality of macrosomia detection at delivery at least in an unselected population. The future aim would be to introduce an automated individual measurement error evaluation to detect the changes

associated with an unacceptable rate of unfavourable outcomes and therefore improve the sonographic accuracy.

## **2. Introduction**

The incidence of fetal macrosomia has been increasing during the last decades (35, 36) although it varies in different countries and have become a great challenge for clinicians (7, 17).

Fetal macrosomia usually is defined as an infant birth weight  $\geq 4000\text{g}$ . It is associated with an increase of various perinatal complications such as perinatal mortality, asphyxia, meconium aspiration, prolonged labor, shoulder dystocia, soft tissue trauma, humeral and clavicular fractures, brachial plexus and facial palsies (1, 32, 34, 38). Mothers who deliver macrosomic infants are at increased risk for anal sphincter laceration (44) and eventually for pelvic floor morbidity in later life (13). On the other hand, an increased risk of the cesarean delivery is emphasized to be the primary maternal risk factor associated with macrosomia (6). Therefore an accurate prenatal prediction of macrosomia would be very useful for planning labor and delivery strategies. Unfortunately, the accuracy level of birth weight estimation both by clinical and sonographic measures is still relatively low, even with modern ultrasound equipment (17, 21). Ultrasound tends to underestimate the weight of macrosomic fetuses and to overestimate in fetuses of less than 4000g (21). This situation may cause potential harm when macrosomia is missed and even more may increase the number of unnecessary interventions such as elective cesarean sections when macrosomia is wrongly suspected (11, 37, 46). The intention to reduce the amount of interventions along with avoiding adverse events is widely spread (25). Although it has been reported that the amount of perinatal complications differs according to the mode of delivery of a macrosomic infant, there is still little evidence that the delivery method has an influence on the perinatal mortality (5). The study of Sandmire and DeMott (42) even supported the fact that rates of perinatal mortality and admission to the neonatal intensive care unit were significantly higher among the macrosomic infants delivered by cesarean section compared to the ones delivered vaginally. It has been announced that prevention of a single brachial plexus injury costs several million \$ and does not bring any cost - benefit (40). Nevertheless, up to 90% of these nerve lesions recover spontaneously (2).

The other approach concerning this problem is that inaccurate fetal weight estimation reduces the possibility of the parents to take part in choosing the route of delivery. They are not informed about the possible adverse events and not familiarized with the current situation.

The sonographic fetal weight estimation has been shown to be more accurate to the clinical weight estimation (14). The fetal weight formulas that are routinely used, appear to be currently available best tools for the accurate detection of fetal macrosomia (10). Indeed, ultrasound biometric measurements and regression equations can determine the fetal weight objectively (8, 9, 16). There has been an effort to try to assess the risk of macrosomia by taking into account other known risk factors, especially in primary care units where symphysial - fundal height is often held as a first predictor of macrosomia. Thus it has been shown that symphysial - fundal height measurements slightly increase suspicion of macrosomia, particularly when adjusted for physiological variables (15). However, others claim estimation of the fetal weight by symphysial - fundal height to be an unreliable method due to the variability in a patient's body mass, height (20), parity or sex of the infant (30). As a consequence, some investigators tried to combine additional clinical and maternal data, considered as risk factors, in the hope for a better estimation of fetal macrosomia. As such, M. Mongelli and J. Gardosi (29) suggested that maternal size, parity and ethnicity should be considered when fetal growth is assessed because these characteristics correlated positively with fetal weight in the third trimester.

Recently, two groups have proposed that a combination of sonographic and pregnancy specific data would be superior to ultrasound alone for prediction of fetal macrosomia at delivery. As such, Mazouni et al. (26) developed and internally validated a specific nomogram for the prediction of macrosomia that combines sonographically estimated fetal weight (EFW) with clinical and demographic data. Applying this method for a selected population with suspected fetal macrosomia according to symphysial - fundal height measurements, they obtained very promising results. Furthermore, Nahum and Stanislaw (31) suggested several equations to predict macrosomia including sonographic data and different combinations of pregnancy specific variables.

This study was conducted to find out, whether the sonographic assessment of fetal weight at term or near term has an influence on the mode of delivery. Concomitantly the predictive quality of the recently suggested combined diagnostic methods have been analyzed in comparison to the sonographic weight estimation alone in an unselected population.

### 3. Patients and methods

#### **I part. Sonographic prediction of fetal macrosomia and effect on the mode of delivery**

The study population that was retrospectively analyzed in the first part of the whole investigation included 3435 pregnant women, who delivered at the University Hospital of Zurich in 2004 – 2007 term, singleton, live born infants where fetal weight was estimated by ultrasound within 7 days prior to delivery.

This study population was divided into 4 groups according to the estimated fetal weight and regarding the birth weight. I group (n=153) consisted of fetuses with diagnosed and after birth confirmed macrosomia (true positive); II group (n=211) included macrosomic infants, where the fetal weight had been underestimated before delivery (false negative); III group (n= 82) consisted of fetuses who were falsely diagnosed as being macrosomic (false positive) and IV group (n= 2989) included normal weight fetuses where macrosomia had been truly ruled out (true negatives).

Macrosomia was defined as an infant birth weight  $\geq 4000\text{g}$ .

The fetal weight was estimated in 3064/3435(89%) fetuses using Hadlock's 3 parameter formula that included the abdominal circumference (AC), the head circumference (HC) and the femur length (FL):

$$\text{Log}_{10}\text{EFW}=1.326 - 0.00326*\text{AC}*FL+0.0107*\text{HC}+0.0438*\text{AC}+0.158*FL.$$

Hadlock's 2 parameter formula:  $\text{Log}_{10}\text{EFW}=1.304+0.05281*\text{AC}+0.1938*FL-0.004*\text{AC}*FL$  was used in 371/3435 (11%) fetuses, when the fetal head parameters could not be accurately obtained (16).

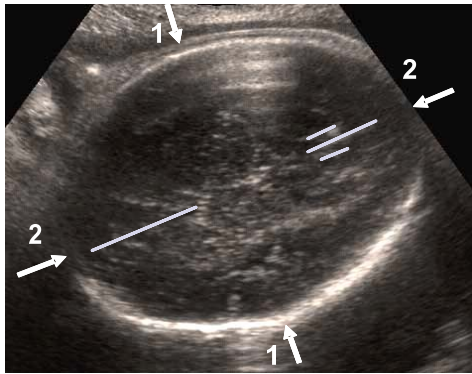
According to the technique used by J. Kurmanavicius et al. (22) all fetal head measurements: biparietal diameter (BPD), occipito - frontal diameter (OFD) and HC were made at the reference plane where the continuous midline echo is broken by the cavum septum pellucidum in the anterior third. Measurements of BPD were made from the fetal skull skin to fetal skull skin. The OFD was measured in the same plane between the leading edge of the frontal bone and the outer border to the occiput (Figure 1). The head circumference was estimated from the measurement of the OFD and BPD using the formula for an ellipse:

$$\text{HC} = 3.14\sqrt{(\text{BPD}^2+\text{OFD}^2)/2}.$$

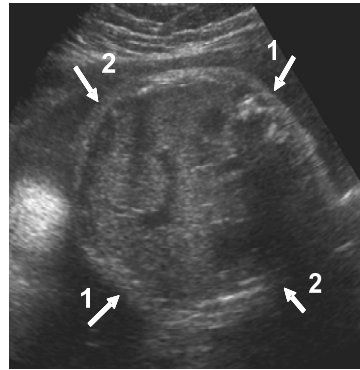
Fetal abdominal transverse diameter (ATD) and abdominal anterior - posterior diameter (AAP) were measured in the plane from the outer edges of the fetal abdominal wall. The correct section was determined by the portion of the umbilical vein situated most centrally as

it enters the portal system within the liver (23) (Figure 2). The AC was then calculated using the formula:  $AC = 3.14 (ATD + AAP)/2$ .

The femur length was measured, after the long axis of the fetus was found and the femur identified as the single long bone at its caudal end (23) (Figure 3).



**Figure 1.** Measurement of head circumference  
BPD = 1-1; OFD = 2-2



**Figure 2.** Measurement of abdominal circumference  
AAP = 1-1; ATD = 2-2



**Figure 3.** Measurement of femur length

## **II part. Sonographic prediction of fetal macrosomia can not be improved by the combination with pregnancy specific characteristics**

The study population, which was investigated in the second part of this study, included 1062 women of European origin, who delivered at the University Hospital of Zurich in 2006. Inclusion criteria were all life born, singleton, term ( $\geq 37$  weeks of gestation) deliveries with a routine EFW obtained by ultrasound and maternal BMI documentation within the last 7 days prior to delivery. Infants with congenital malformations and hydrops fetalis were excluded from the study.

The fetal weight was estimated in 924/1062 (87%) fetuses using Hadlock's 3 parameter formula. In 138/1062 (13%) fetuses Hadlock's 2 parameter formula was used.



The accuracy of the sonographic fetal weight estimations was additionally assessed by calculating the percentage error (PE)  $((EFW-BW) / BW * 100\%)$  and the absolute percentage error (APE) between estimated fetal and birth weight.

The nomogram published by Mazouni et al. (26) included the following variables: parity, ethnicity, maternal body mass index (BMI) at delivery and presence of fetal macrosomia estimated by ultrasound. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of these methods were calculated. As the cut-off level of probability was not available for the study of Mazouni et al. (26), different cut-off levels of probability were applied to predict macrosomia (50%, 70%, 90%, 100%) when analyzing this nomogram.

The three equations producing rather impressive and accurate results for the prediction of macrosomia as suggested by Nahum and Stanislaw (31) involved the following variables: gestational age at delivery (GA), maternal height (Ht), maternal weight at 26 weeks (Wt<sub>182</sub>), maternal third trimester weight gain rate (Rate<sub>3rd</sub>), prior parity, fetal AC, biparietal diameter (BPD) and the interval between the ultrasound examination and delivery ( $\Delta$ US).

The equations [3], [4] and [11], respectively (31):

$$[3] \text{EBW} = -3468 + (10.95 * \text{AC}) + (28.83 * \text{BPD}) + (19.86 * \Delta\text{US}) + (0.00007464 * \text{GA} * \text{Ht} * \text{Wt}_{182}) + (3.336 * \text{GA} * \text{Rate}_{3rd} * [\text{Parity} + 1])$$

$$[4] \text{EBW} = -3337 + (10.96 * \text{AC}) + (27.61 * \text{BPD}) + (20.16 * \Delta\text{US}) + (0.0001027 * \text{GA} * \text{Ht} * \text{Wt}_{182})$$

$$[11] \text{EBW} = -1627 + (13.18 * \text{AC}) + (16.23 * \Delta\text{US}) + (0.00009964 * \text{GA} * \text{Ht} * \text{Wt}_{182}) + (3.173 * \text{GA} * \text{Rate}_{3rd} * [\text{Parity} + 1])$$

were analyzed in a subgroup of n=303 women of the initial study group (n=1062) for which complete data was available.

A cut-off value of 3830g for the fetal weight estimation was used when testing the equations suggested by Nahum and Stanislaw (31). Receiver-operating characteristics (ROC) curves were generated to compare the combined methods with ultrasound alone.

### **Statistical analysis**

All statistical analysis was carried out with SPSS for Windows (version 15.0, SPSS Inc., Chicago, IL). Mean values of two groups were compared using two sample t test and X<sup>2</sup> test for the comparison of proportions. Additionally, the X<sup>2</sup> test was completed by Post Hoc Cell analysis with the Wilson test. P < 0.05 was considered statistically significant.

## 4. Results

### I part. Sonographic prediction of fetal macrosomia and effect on the mode of delivery

In the recent part of the study data from 3435 pregnancies was reviewed. This study population included 364 (10.6%) macrosomic newborns within the mean BW  $3404 \pm 471$ g and mean EFW  $3279 \pm 475$ g. Details are described in Table 1.

**Table 1.** Characteristics of the study population analyzed in part I of the investigation.

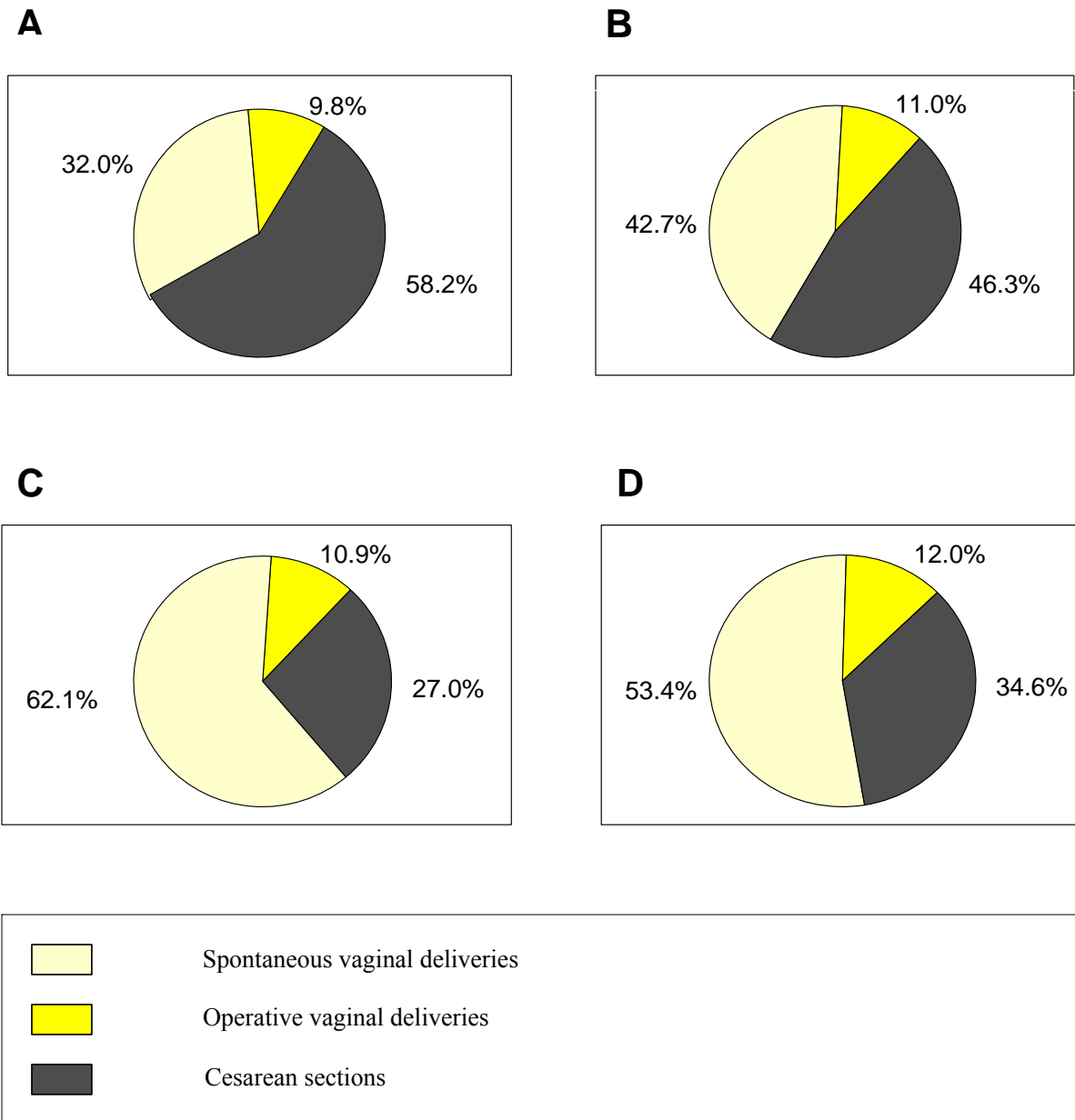
Characteristics	n (%), mean $\pm$ SD  (n=3435)
Macrosomic newborns	364 (10.6)
Macrosomia sonographically predicted	235 (6.8)
Gestational age at delivery (weeks)	$39 \pm 1.2$
Birth weight (g)	$3404 \pm 471$
Sonographically estimated fetal weight (g)	$3279 \pm 475$
Parity:	
Primiparous	1688 (49.1)
Multiparous	1747 (50.9)

Table 2 presents division of the population into four groups according to EFW and confirmation of the diagnosis of macrosomia after birth. No significant difference has been noted between EFW and BF in the group of the true macrosomic infants. However, it has been observed in the remaining groups of infants.

**Table 2.** The difference between means of the fetal weight estimated by ultrasound and birth weight of infants in the four formatted groups.

Study group	Estimated fetal weight by ultrasound (g)	Birth weight (g)	P - value
True positive (n = 153)	4319 ± 239	4322 ± 223	0.9
False negative (n= 211)	3665 ± 240	4184 ± 149	<0.0001
False positive (n= 82)	4154 ± 115	3772 ± 169	<0.0001
True negative (n=2989)	3175 ± 393	3291 ± 384	<0.0001

A cesarean section has been performed in 58.2% of pregnant women, where fetal macrosomia was truly ruled in (true positive) and for 34.6% of women who delivered normal weight infants (true negative). An overestimation of fetal weight (false positive) led to the 46.3% rate of cesarean sections. However, cesarean section was chosen only in 27.0% of false negative cases where fetal weight was underestimated (Figure 4).

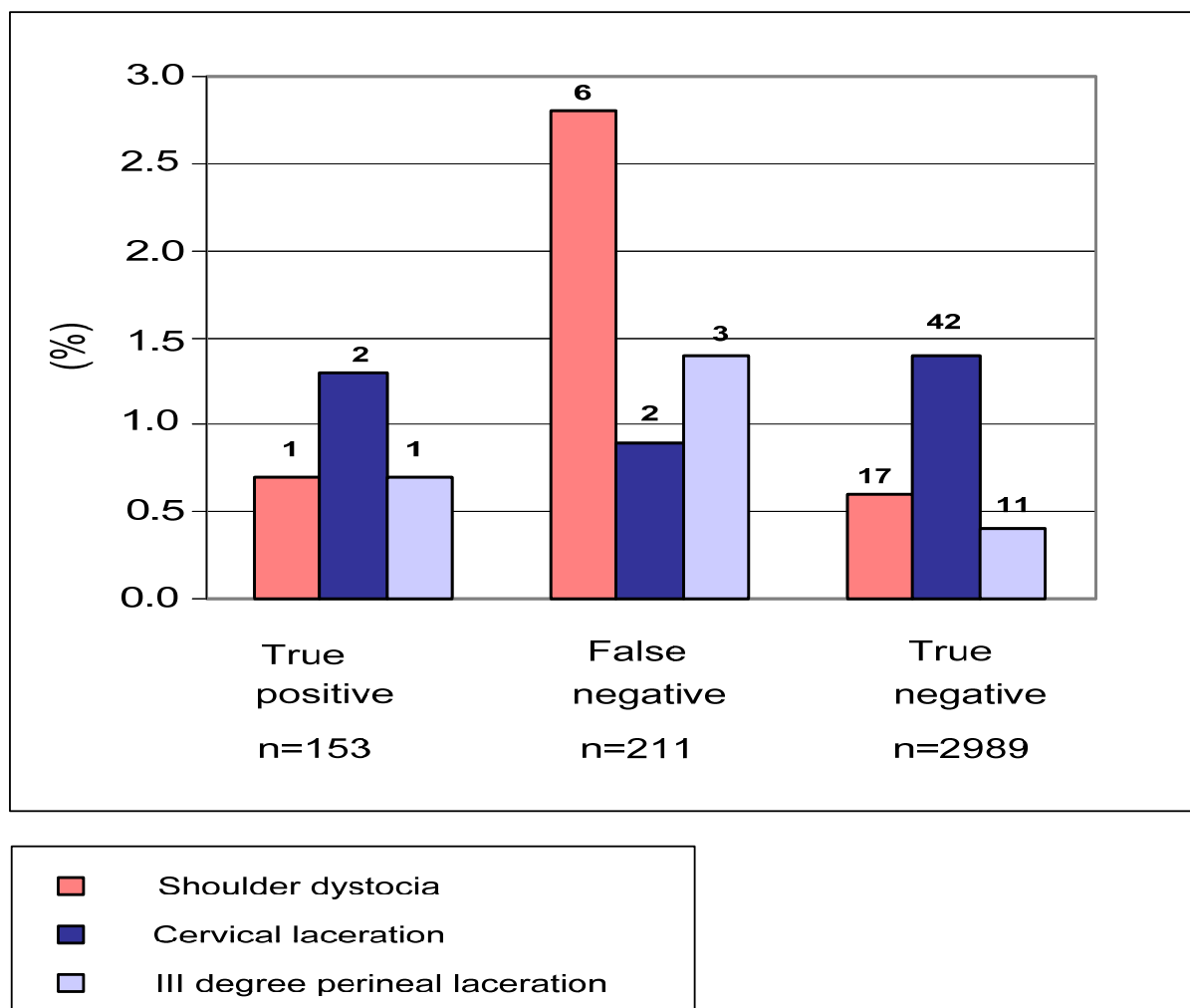


**Figure 4.** The relationship between estimated fetal weight and the mode of delivery. A: True positive infants n=153; B: False positive infants n= 82; C: False negative infants n= 211; D: True negative infants n= 2989.

The hypothesis that there is no relationship between the formatted groups and the mode of delivery was rejected because employing the  $X^2$  test, the P value was  $<0.0001$  confirming that the relationship was extremely significant. Additionally the Post Hoc Cell analysis with the Wilson test was applied. It proved significantly different proportions of cesarean section distribution in the four groups. Furthermore, the difference of proportions of the cesarean section rate between the true positive and the false negative group was equal 0.31 (CI 95%, 0.21 - 0.4), ( $P < 0.0001$ )

and greater than that between the false positive and the true negative group 0.12 (CI 95% 0.01 - 0.23).

Figure 5 presents the fetal and maternal complications that occurred during a vaginal delivery. No unfavourable outcomes that could have occurred in the group of false positive infants have been noticed. The highest incidence of shoulder dystocia (n=6) was in the false negative group though it was not significantly different from the other groups. Even though the proportion of cervical laceration was the highest in the group of normal weight infants (n=11), it was not statistically significant.



**Figure 5.** Complications of vaginal delivery.

To compare the complications in macrosomic and non macrosomic infants after birth, there were overall significantly more cases of shoulder dystocia in the macrosomic group,

( $P=0.007$ ). Third degree perineal lacerations occurred more often in mothers who delivered macrosomic infants, although not significantly.

**II part. Sonographic prediction of fetal macrosomia can not be improved by the combination with pregnancy specific characteristics**

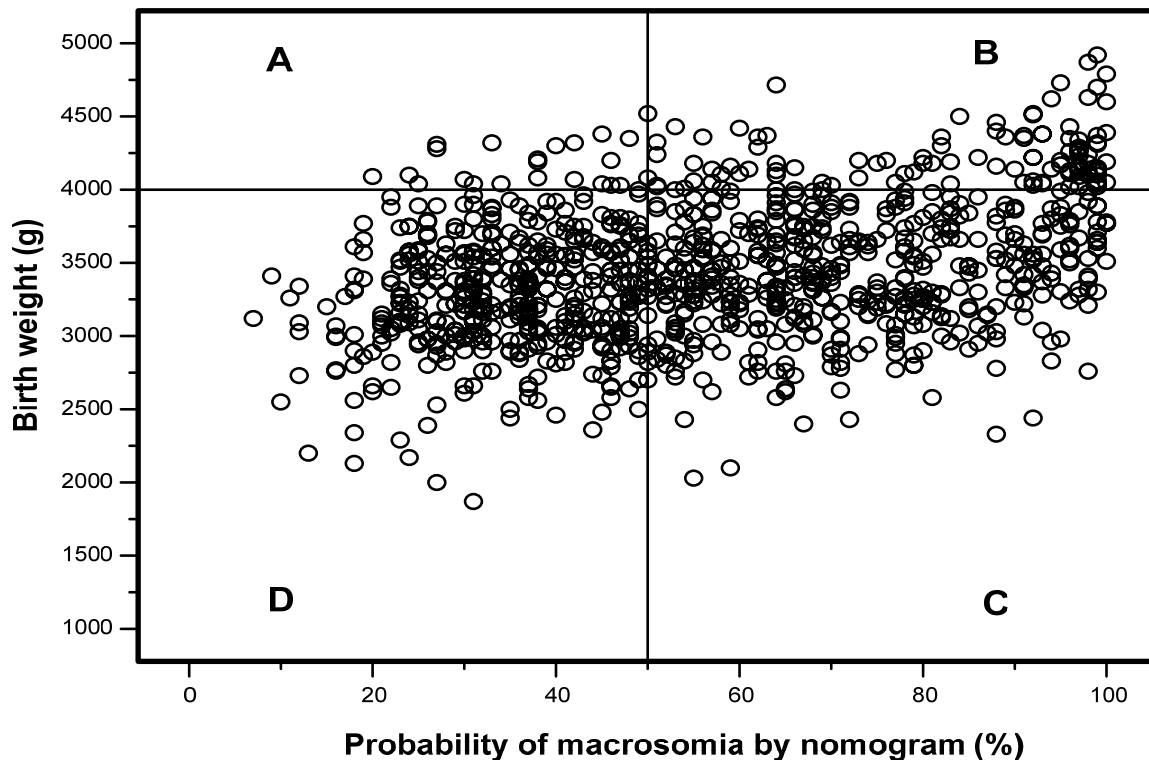
1062 singleton pregnancies were analyzed in the current part of the study. Macrosomia was present in 135 newborns (12.7%). The mean EFW was  $3323 \pm 474\text{g}$  (range, 1614 - 5076g) and macrosomia was sonographically predicted in 85 fetuses (8.0%). In a sub-group of 303 pregnancies that met the criteria required for the equations of Nahum and Stanislaw (31) , macrosomia presented in 34 newborns (11.2%) and was predicted by ultrasound in 16 infants (5.3%). The main study group and the subgroup, where different methods to improve detection of fetal macrosomia were applied, appeared to be statistically equal as  $P>0.05$ . The characteristics of the study populations are given in Table 3.

**Table 3.** Characteristics of the study population: I- study population, to which the Mazouni et al. (26) nomogram was applied; II- a subgroup, to which the Nahum and Stanislaw (31) equations were applied.

Characteristics	I	II	P-value
	n (%), mean $\pm$ SD (n=1062)	n (%), mean $\pm$ SD (n=303)	
Macrosomic newborns	135 (12.7)	34 (11.2)	0.49
Macrosomia sonographically predicted	85 (8.0)	16 (5.3)	0.13
Gestational age at delivery (weeks)	39.3 $\pm$ 1.2	39.1 $\pm$ 1.2	0.05
Birth weight (g)	3437 $\pm$ 459	3399 $\pm$ 472	0.21
Sonographically estimated fetal weight (g)	3323 $\pm$ 474	3296 $\pm$ 490	0.38
Maternal age (years)	30 $\pm$ 5.8	29.4 $\pm$ 5.7	0.36
Maternal BMI at delivery	28.5 $\pm$ 4.2	28.6 $\pm$ 4.5	0.58
Parity:			
Primiparous	560 (52.7)	152 (50.2)	0.43
Multiparous	502 (47.3)	151 (49.8)	0.43

The calculation of the mean percentage error (PE) between sonographic weight estimation and the birth weight revealed only a slight underestimation of the birth weight ( $-3.06 \pm 8.36$  %). The absolute percentage error (APE) revealed a mean deviation of the sonographically estimated fetal weight from birth weight of  $3.05 \pm 8.06$ %.

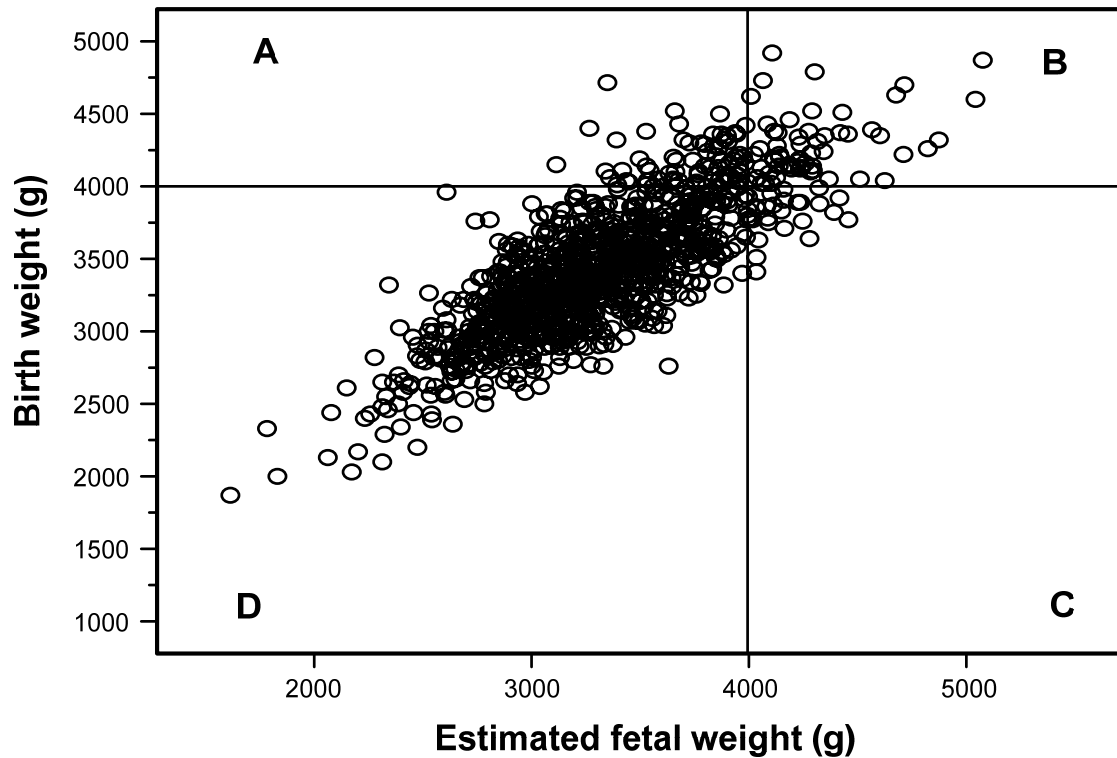
Plotting the birth weights against the calculated probability of macrosomia derived from the nomogram of Mazouni et al. (26) revealed a horizontal scatter leading to a high proportion of false positive test results (53%, n= 491) when the threshold to diagnose macrosomia ( $\geq 4000\text{g}$ ) was set at a 50% probability level (false negative: 16%, n=22) (Figure 6).



**Figure 6.** Relation between birth weight (g) and the calculated macrosomia probability (%) of the Mazouni et al. nomogram (26). The threshold to predict macrosomia was set at 50% for nomogram probability at a birth weight of  $\geq 4000\text{g}$ . A: false negative (n= 22); B: true positive (n= 113); C: false positive (n= 491); D: true negative (n= 436).

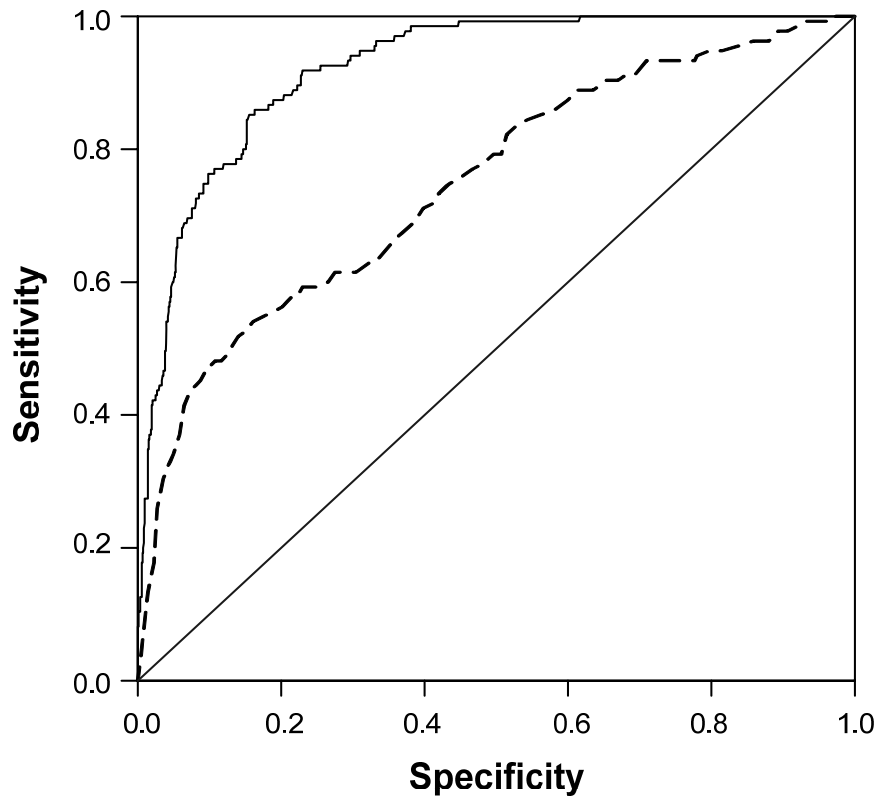
In contrast, when sonographic estimation of fetal weight alone was plotted against birth weight, the scatter showed a diagonal course leading to significantly less false positive results ( 3%, n= 26) however, at the cost of an increase in false negative results (56%, n= 76) (Figure 7).





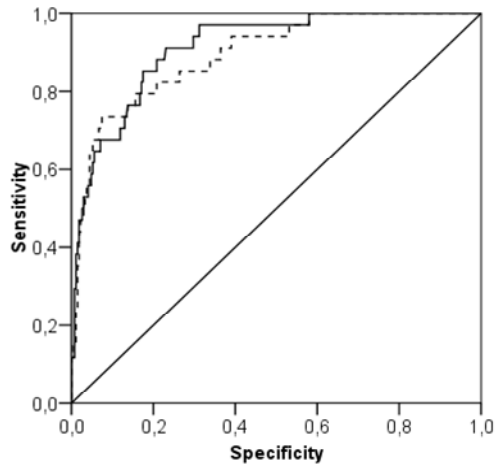
**Figure 7.** Relation between birth weight (g) and estimated fetal weight (g) by ultrasound alone. The threshold to predict macrosomia was set at  $\geq 4000$ g for estimated fetal and birth weight. A: false negative (n= 76); B: true positive (n= 59); C: false positive (n= 26); D: true negative (n= 901).

ROC curve analysis revealed a significantly higher AUC for sonographic macrosomia prediction alone 0.922 (CI 95%: 0.902-0.943) when compared to the suggested combined nomogram of Mazouni et al. (26) 0.747 (CI 95%, 0.700-0.794), ( $P < 0.0001$ ) (Figure 8).

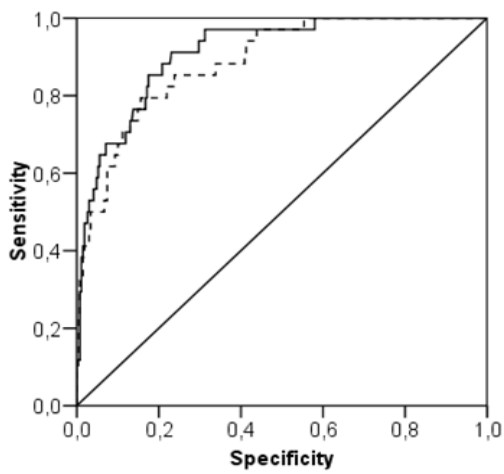


**Figure 8.** Receiver-operating characteristics (ROC) curves to predict macrosomia by ultrasound alone ( — AUC= 0.922) and the combined method nomogram of Mazouni et al. (26) (--- AUC= 0.747).

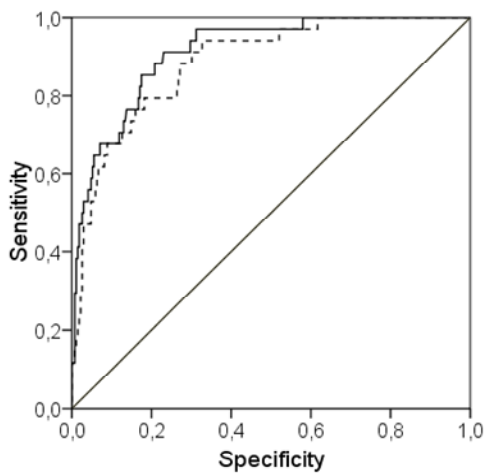
In ROC curve analysis AUC of the Nahum and Stanislaw (31) equations was similar but not superior to ultrasound alone (AUC 0.895 (CI 95% 0.839-0.950) [3], (AUC 0.887 (CI 95% 0.834-0.941) [4], (AUC 0.885 (CI 95% 0.831-0.940) [11], vs. 0.912 (CI 95% 0.867-0.958) ( $P<0.0001$ ), respectively, (Figure 9).



[3]



[4]



[11]

**Figure 9.** Receiver-operating characteristics (ROC) curves to predict macrosomia by ultrasound alone (— AUC=0.912) and the combined equations of Nahum and Stanislaw (31) [3] (--- AUC= 0.895); [4] (--- AUC= 0.887); [11] (--- AUC= 0.885).

Test quality was analyzed at different cut-off values for the Mazouni et al. (26) nomogram and compared with sonographic macrosomia prediction alone. It revealed that accuracy of sonographic prediction alone was higher than the combined method nomogram at any probability cut-off level (Table 4).

**Table 4.** Comparison of the Mazouni et al. (26) nomogram at different probability cut-off levels and ultrasound alone macrosomia estimates.

Cut-off	Sensitivity (%)	Specificity (%)	PPV (%)	PV (%)	Accuracy (%)
100%	3.7	99.6	55.6	87.7	87.4
90%	44.4	91.9	44.4	91.9	85.9
70%	60.0	73.5	24.8	92.7	71.8
50%	83.7	47.0	18.7	95.2	51.7
Ultrasound $\geq$ 4000g	43.7	97.2	69.4	92.2	90.4

The accuracy, PPV and specificity of the equations proposed by Nahum and Stanislaw (31) was quite similar to ultrasound alone, however did not prove to be superior (Table 5).

**Table 5.** Comparison of the combined Nahum and Stanislaw equations (31) and ultrasound alone macrosomia estimates.

Method	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Equation 3	67.7	92.6	51.2	96.2	90.1
Equation 4	58.1	93.4	50.0	95.0	89.8
Equation 11	41.9	97.4	65.0	93.6	91.7
Ultrasound $\geq 4000\text{g}$	71.0	91.9	50.0	96.5	89.8

## 5. Discussion

The findings of this investigation show that fetal macrosomia appears to be associated with vast variety of problems not only for the obstetrician but also for the pregnant woman. Evidence is emerging that it is extremely difficult to choose the best mode of delivery when fetal macrosomia is predicted. It does not appear rational that routine elective cesarean delivery for suspected macrosomia should be employed in the general population, however, vaginal delivery of an overgrown fetus requires attention and preparedness (17). As the accuracy of sonographic prediction of fetal macrosomia has been disappointing and even resulting in the cesarean delivery of non macrosomic infants (45), this study has been conducted to evaluate the predictive quality of promising new methods combining ultrasound with pregnancy specific data to detect fetal macrosomia in an unselected population. It has revealed that a simple routine sonographic estimation provides equal, if not more precise information, though it is still not satisfactory enough.

Clinical estimation of fetal weight is hampered by several maternal characteristics such as obesity (4), height (20), parity or sex of the infant (30) making this method unreliable. On the other hand, obtaining an accurate fetal biometry in late pregnancy near term could be rather difficult as measurements in reference planes due to a low position of the fetal head which becomes engaged or oligohydramnion can be quite challenging (12, 28). In fact, none of the widely used sonographical, clinical or demographical methods is a precise and reliable determinant of a macrosomic fetus.

Results of the study have proved the hypothesis that the inappropriate prediction of fetal weight has influence on the mode of delivery. The proportion of cesarean sections performed in the group of pregnant women where macrosomia had been falsely ruled out appeared to be twice smaller in comparison with true macrosomic infants. One could consider this fact as a suggestion to provide an expectant management of delivery for a macrosomic fetus, although there is insufficient evidence about the threshold of the estimated fetal weight that should prompt a cesarean delivery (7). It has been even suggested, that if pregnancy is not complicated by diabetes or there are no other contraindications, elective cesarean section should not be the first choice of management even when macrosomia is diagnosed by ultrasound (24, 39). The overestimation of the fetal weight significantly increases the incidence of cesarean section in comparison with the group of normal weight fetuses. Therefore, the speculation of Weeks et al. (45) that anticipation of a macrosomic infant may have influenced the aggressiveness of intrapartum management seems to be quite reasonable.

However, it is necessary to mention that pelvic anatomy of a mother is another determining factor in choosing the route of delivery. Thus clinicians should be very thoughtful when planning the most suitable mode of delivery and take into account the fetal weight, maternal constitution, obstetric history, progression during labor and other evidence suggestive of fetopelvic disproportion (48).

The rate of operative vaginal deliveries was around 11% and no significant difference was noticed between the formatted groups. This mode of delivery did not increase the amount of fetal or maternal complications, though Kolderup et al. (19) had reported that forceps delivery was associated with a higher risk of persistent injury compared to spontaneous vaginal or cesarean delivery. However, it is known that a vaginal delivery possesses a greater risk of such complications as shoulder dystocia, III degree perineal or cervical lacerations (44). Although the incidence of adverse events almost did not differ in our study population because of inaccurate fetal weight estimation. Slightly more cases of shoulder dystocia have been observed in the group where macrosomia had been falsely ruled out (false negative) (Figure 5). It might have happened that the care of delivery was not fully efficient in those cases.

The comparison of all macrosomic and non macrosomic infants after birth significantly revealed again the greater amount of shoulder dystocia in the macrosomic group. The mothers of heavier babies suffered from the third degree perineal lacerations more often, although not significantly.

The evidence is emerging that an accurate fetal weight estimation and in particular, the detection of macrosomia could lead to a better and more optimal outcome for a mother and her infant. As a matter of fact, it would help clinicians to provide parents with more accurate prognosis regarding the complications associated with the route of delivery and to have them participate in the process of taking a decision.

It is extremely important to comply with certain rules while performing fetal biometry by ultrasound: a) adequate magnification and power of the signal, b) correct reference plane and angle, c) correct and precise calliper placement and their fitting around the fetal outline, d) validity of measurement charts for local methods and population (43) (Figures 1, 2, 3).

We have tried to employ the proposed model of Mazouni et al. (26) and the equations of Nahum and Stanislaw (31) for prediction of macrosomia in this unselected population.

Mazouni et al. (26) found greater accuracy of fetal macrosomia prediction where sonographic measurements in combination with parity and ethnicity were used as when ultrasound alone was performed. The reported values for sensitivity and specificity were around 80%. It is not

clear, however, which probability cut-off levels were applied in that study, and, as can be seen in Table 4, these have a considerable impact on the accuracy of prediction. Thus, applying the proposed model to our unselected population, the accuracy of predicting macrosomia at a cut-off level of 50% was distinctly lower than ultrasound alone (51.7 vs. 90.4, respectively). Even when increasing the cut-off to 100%, the accuracy was still lower than that of ultrasound alone and sensitivity was poor. One reason for these differing findings may be due to the fact, that the model of Mazouni et al. (26) was developed in a pre-selected population referred for suspected macrosomia based on a suspicious symphysial-fundal measurement leading to the incidence of macrosomia of 55.6 %. Thus, this method may not be applied to a general population and even more, it is not known how many fetuses with macrosomia had been missed due to the selection criteria. Indeed, the sensitivity to detect macrosomic fetuses by symphysis-fundus measurement is rather poor (20).

According to the results of this study in an unselected population, the PPV of ultrasound alone was distinctly higher (69.4%) compared to the PPV of the Mazouni et al. (26) nomogram (18.7%). The NPV of ultrasound alone was 92.2%, which suggests, that only 8% of normal weighting fetuses would be determined as macrosomic. The true value of the ultrasound in fetal weight estimation, however, might be its ability to rule out the diagnosis of macrosomia to prevent unnecessary interventions (3). In the analyzed collective, application of the combined method of Mazouni et al. (26) revealed 53% false positive test results (probability cut-off 50%) compared to only 2.8% false positive test results with ultrasound alone.

The ROC curve analysis revealed both methods to be statistically useful, because AUC was more than 0.5. Nevertheless, AUC of macrosomia detection using ultrasound alone was significantly greater than AUC of the Mazouni et al. (26) nomogram, implicating this method to be insufficient at least in our collective.

When testing the macrosomia prediction equations of Nahum and Stanislaw (31), the suggested best performing equations did not appear to be superior to ultrasound estimation alone (Table 5). ROC curve analysis proved that fetal weight estimation based on ultrasound alone was slightly better than the proposed equations (Figure 9). It is not clear why women with gestational diabetes were excluded in the study of Nahum et Stanislaw (31) since this group is especially at risk for macrosomia and delivery associated complications (18). One reason might be that sonographic weight estimations were performed up to 11 weeks before delivery. A considerable amount of macrosomia, however, appears in the last trimester of pregnancy, especially in diabetic women (27). One would have expected the predictive quality of the combination equations rather to increase when including sonographic weight



estimations closer to delivery (within 7 days as in our study). This was not the case, and predictive measures of the Nahum and Stanislaw equations were similar to ultrasound alone.

The application of sonographic weight estimation as well as the prediction of macrosomia solely from maternal and pregnancy specific characteristics has been shown to provide comparable, however, not satisfactory accuracy (31). It was the hope that a combination of these functionally independent measures would increase the quality of macrosomia prediction. According to the findings of the study, it is not convincing that this method would be superior to sonographic prediction of macrosomia alone at least in an unselected population. It appears that ruling out macrosomia is even more important than detection in order to avoid unnecessary procedures such as cesarean sections or induction of labour (37).

It is important to note that the results do not favour ultrasound alone to a combination method due to unusually high sonographic detection rates of macrosomia in the study collective. In fact, the prediction rate in the Obstetric Clinic of Zurich University Hospital was in an average range when compared to the literature (7).

To sum up, it is reasonable to state that fetal weight estimation before delivery has a great impact on the method of delivery chosen by the obstetrician. The related errors hamper selection of the optimal mode and could lead to the increased amount of unfavourable events to a mother and to an infant.

I agree with the opinion that the error associated with sonographic estimations of fetal weight at term reduces its value (33); nevertheless, sonography appears still to be one of the best and most objective methods for birth weight estimation currently available and a combination with pregnancy specific data does not improve the predictive quality of macrosomia detection at delivery. It is suggested that new strategies should be implemented in order to make sonography more accurate and precise. One important future objective might be an automated individual measurement error evaluation, applying the particular tool "The cumulative sum chart" (CUSUM) (47), to improve sonographic accuracy as well as clinical competence by providing an early warning of an adverse trend (43). Furthermore, it could be introduced for monitoring of trainees learning the ultrasound (41).

## 6. References

1. Adesina OA, Olayemi O. Fetal macrosomia at the University College Hospital, Ibadan: a 3-year review. *J Obstet Gynaecol* 23 (1): 30-3, 2003.
2. Antoniadis G, Konig RW, Mohr K, Kretschmer T, Richter HP. [Management of obstetrical brachial plexus palsy--own experience with the primary operative technique]. *Handchir Mikrochir Plast Chir* 35 (2): 98-105, 2003.
3. Ben-Haroush A, Yogev Y, Hod M. Fetal weight estimation in diabetic pregnancies and suspected fetal macrosomia. *J Perinat Med* 32 (2): 113-21, 2004.
4. Blann DW, Prien SD. Estimation of fetal weight before and after amniotomy in the laboring gravid woman. *Am J Obstet Gynecol* 182 (5): 1117-20, 2000.
5. Boulet SL, Salihi HM, Alexander GR. Mode of delivery and birth outcomes of macrosomic infants. *J Obstet Gynaecol* 24 (6): 622-9, 2004.
6. Chatfield J. ACOG issues guidelines on fetal macrosomia. American College of Obstetricians and Gynecologists. *Am Fam Physician* 64 (1): 169-70, 2001.
7. Chauhan SP, Grobman WA, Gherman RA, Chauhan VB, Chang G, Magann EF, Hendrix NW. Suspicion and treatment of the macrosomic fetus: a review. *Am J Obstet Gynecol* 193 (2): 332-46, 2005.
8. Chauhan SP, West DJ, Scardo JA, Boyd JM, Joiner J, Hendrix NW. Antepartum detection of macrosomic fetus: clinical versus sonographic, including soft-tissue measurements. *Obstet Gynecol* 95 (5): 639-42, 2000.
9. Combs CA, Jaekle RK, Rosenn B, Pope M, Miodovnik M, Siddiqi TA. Sonographic estimation of fetal weight based on a model of fetal volume. *Obstet Gynecol* 82 (3): 365-70, 1993.
10. Conway DL. Delivery of the macrosomic infant: cesarean section versus vaginal delivery. *Semin Perinatol* 26 (3): 225-31, 2002.

11. Coomarasamy A, Connock M, Thornton J, Khan KS. Accuracy of ultrasound biometry in the prediction of macrosomia: a systematic quantitative review. *Bjog* 112 (11): 1461-6, 2005.
12. Cromi A, Ghezzi F, Di Naro E, Siesto G, Bergamini V, Raio L. Large cross-sectional area of the umbilical cord as a predictor of fetal macrosomia. *Ultrasound Obstet Gynecol* 30 (6): 861-6, 2007.
13. Dietz HP, Wilson PD. Childbirth and pelvic floor trauma. *Best Pract Res Clin Obstet Gynaecol* 19 (6): 913-24, 2005.
14. Farrell T, Holmes R, Stone P. The effect of body mass index on three methods of fetal weight estimation. *Bjog* 109 (6): 651-7, 2002.
15. Gardosi J, Francis A. Controlled trial of fundal height measurement plotted on customised antenatal growth charts. *Br J Obstet Gynaecol* 106 (4): 309-17, 1999.
16. Hadlock FP, Harrist RB, Sharman RS, Deter RL, Park SK. Estimation of fetal weight with the use of head, body, and femur measurements--a prospective study. *Am J Obstet Gynecol* 151 (3): 333-7, 1985.
17. Henriksen T. The macrosomic fetus: a challenge in current obstetrics. *Acta Obstet Gynecol Scand* 87 (2): 134-45, 2008.
18. Yang J, Cummings EA, O'Connell C, Jangaard K. Fetal and neonatal outcomes of diabetic pregnancies. *Obstet Gynecol* 108 (3 Pt 1): 644-50, 2006.
19. Kolderup LB, Laros RK, Jr., Musci TJ. Incidence of persistent birth injury in macrosomic infants: association with mode of delivery. *Am J Obstet Gynecol* 177 (1): 37-41, 1997.
20. Kraiem J, Chiha N, Bouden S, Ounaissa F, Falfoul A. [Clinical fetal weight estimation and prediction of macrosomia]. *Tunis Med* 82 (3): 271-5, 2004.

21. Kurmanavicius J, Burkhardt T, Wisser J, Huch R. Ultrasonographic fetal weight estimation: accuracy of formulas and accuracy of examiners by birth weight from 500 to 5000 g. *J Perinat Med* 32 (2): 155-61, 2004.
22. Kurmanavicius J, Wright EM, Royston P, Wisser J, Huch R, Huch A, Zimmermann R. Fetal ultrasound biometry: 1. Head reference values. *Br J Obstet Gynaecol* 106 (2): 126-35, 1999.
23. Kurmanavicius J, Wright EM, Royston P, Zimmermann R, Huch R, Huch A, Wisser J. Fetal ultrasound biometry: 2. Abdomen and femur length reference values. *Br J Obstet Gynaecol* 106 (2): 136-43, 1999.
24. Lim JH, Tan BC, Jammal AE, Symonds EM. Delivery of macrosomic babies: management and outcomes of 330 cases. *J Obstet Gynaecol* 22 (4): 370-4, 2002.
25. Mastrogiannis DS, Knuppel RA. Critical management of the very low birth weight infant and macrosomic fetus. *Clin Perinatol* 23 (1): 51-89, 1996.
26. Mazouni C, Rouzier R, Ledu R, Heckenroth H, Guidicelli B, Gamberre M. Development and internal validation of a nomogram to predict macrosomia. *Ultrasound Obstet Gynecol* 29 (5): 544-9, 2007.
27. Mello G, Parretti E, Mecacci F, La Torre P, Cioni R, Cianciulli D, Scarselli G. What degree of maternal metabolic control in women with type 1 diabetes is associated with normal body size and proportions in full-term infants? *Diabetes Care* 23 (10): 1494-8, 2000.
28. Mongelli M, Chew S, Yuxin NG, Biswas A. Third-trimester ultrasound dating algorithms derived from pregnancies conceived with artificial reproductive techniques. *Ultrasound Obstet Gynecol* 26 (2): 129-31, 2005.
29. Mongelli M, Gardosi J. Longitudinal study of fetal growth in subgroups of a low-risk population. *Ultrasound Obstet Gynecol* 6 (5): 340-4, 1995.
30. Mongelli M, Gardosi J. Symphysis-fundus height and pregnancy characteristics in ultrasound-dated pregnancies. *Obstet Gynecol* 94 (4): 591-4, 1999.

31. Nahum GG, Stanislaw H. A computerized method for accurately predicting fetal macrosomia up to 11 weeks before delivery. *Eur J Obstet Gynecol Reprod Biol* 133 (2): 148-56, 2007.
32. Norwitz ER, Snegovskikh VV, Caughey AB. Prolonged pregnancy: when should we intervene? *Clin Obstet Gynecol* 50 (2): 547-57, 2007.
33. O'Reilly-Green C, Divon M. Sonographic and clinical methods in the diagnosis of macrosomia. *Clin Obstet Gynecol* 43 (2): 309-20, 2000.
34. Oral E, Cagdas A, Gezer A, Kaleli S, Aydinli K, Ocer F. Perinatal and maternal outcomes of fetal macrosomia. *Eur J Obstet Gynecol Reprod Biol* 99 (2): 167-71, 2001.
35. Orskou J, Henriksen TB, Kesmodel U, Secher NJ. Maternal characteristics and lifestyle factors and the risk of delivering high birth weight infants. *Obstet Gynecol* 102 (1): 115-20, 2003.
36. Orskou J, Kesmodel U, Henriksen TB, Secher NJ. An increasing proportion of infants weigh more than 4000 grams at birth. *Acta Obstet Gynecol Scand* 80 (10): 931-6, 2001.
37. Parry S, Severs CP, Sehdev HM, Macones GA, White LM, Morgan MA. Ultrasonographic prediction of fetal macrosomia. Association with cesarean delivery. *J Reprod Med* 45 (1): 17-22, 2000.
38. Piasek G, Starzewski J, Chil A, Wrona-Cyranowska A, Gutowski J, Anisiewicz A, Pejas-Dembowska R, Malmur M, Krawczyk J, Rudzinski R. [Analysis of labour and perinatal complications in case of foetus weight over 4000 g]. *Wiad Lek* 59 (5-6): 326-31, 2006.
39. Rouse DJ, Owen J. Sonography, suspected macrosomia, and prophylactic cesarean: a limited partnership. *Clin Obstet Gynecol* 43 (2): 326-34, 2000.

40. Rouse DJ, Owen J, Goldenberg RL, Cliver SP. The effectiveness and costs of elective cesarean delivery for fetal macrosomia diagnosed by ultrasound. *Jama* 276 (18): 1480-6, 1996.
41. Rozenberg P, Porcher R, Salomon LJ, Boirot F, Morin C, Ville Y. Comparison of the learning curves of digital examination and transabdominal sonography for the determination of fetal head position during labor. *Ultrasound Obstet Gynecol* 31 (3): 332-7, 2008.
42. Sandmire HF, DeMott RK. The Green Bay cesarean section study. IV. The physician factor as a determinant of cesarean birth rates for the large fetus. *Am J Obstet Gynecol* 174 (5): 1557-64, 1996.
43. Ville Y. 'Ceci n'est pas une echographie': a plea for quality assessment in prenatal ultrasound. *Ultrasound Obstet Gynecol* 31 (1): 1-5, 2008.
44. Walsh CA, Mahony RT, Foley ME, Daly L, O'Herlihy C. Recurrence of fetal macrosomia in non-diabetic pregnancies. *J Obstet Gynaecol* 27 (4): 374-8, 2007.
45. Weeks JW, Pitman T, Spinnato JA, 2nd. Fetal macrosomia: does antenatal prediction affect delivery route and birth outcome? *Am J Obstet Gynecol* 173 (4): 1215-9, 1995.
46. Weiner Z, Ben-Shlomo I, Beck-Fruchter R, Goldberg Y, Shalev E. Clinical and ultrasonographic weight estimation in large for gestational age fetus. *Eur J Obstet Gynecol Reprod Biol* 105 (1): 20-4, 2002.
47. Williams SM, Parry BR, Schlup MM. Quality control: an application of the cusum. *Bmj* 304 (6838): 1359-61, 1992.
48. Zamorski MA, Biggs WS. Management of suspected fetal macrosomia. *Am Fam Physician* 63 (2): 302-6, 2001.

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