Fetal Abdominal Subcutaneous Tissue Thickness (FASTT): Correlation with Other Biometric Measurements and Neonatal Outcomes in a Sample Population of Filipino Fetuses

GRACE DL. VALDECANTOS, MD and MA. JOSEFINA PAGUIRIGAN-KAYABAN, MD, FPOGS

Department of Obstetrics and Gynecology, De Los Santos - STI Medical Center

Current parameters to measure fetal size may not accurately identify those fetuses at nutritional risk. Ultrasound-generated estimates of fetal fat may be useful in the evaluation of fetal growth abnormalities.

Objectives: To determine the correlation of fetal abdominal subcutaneous tissue thickness at term with other biometric measurements and neonatal outcome.

Methodology: Included were women with term singleton pregnancies within one week of delivery at the Department of Obstetrics and Gynecology. Excluded were women whose fetuses had congenital anomalies. Maternal age, gravidity, menstrual age at time of scan and presence of maternal complications were documented. Thickness of the subcutaneous fat tissue at the anterior abdominal wall was measured sonographically by board certified obstetrician sonologists and correlated with BPD, HC, AC, SEFW and actual birthweight using Pearson’s correlation coefficient and linear regression. T-test and ROC analysis were also done. For all tests, a 95% confidence level was considered significant.

Results: FASTT was significantly correlated with AC, SEFW and actual birthweight. LGAs had significantly thicker FASTT than AGAs. Accuracy of FASTT in predicting a CS mode of delivery, with a cutoff of <5.4mm was low (47.5% sensitivity), while ability to predict NSD was high at 82.7%.

Conclusion: FASTT can be a good parameter for estimation of fetal size, but may not be able to predict a CS mode of delivery.

Key words: fetal abdominal subcutaneous tissue thickness, small for gestational age, large for gestational age

Fetal growth is a result of complex interactions between several maternal, fetal and placental mechanisms. A final classification of neonatal growth outcome depends on how this development is defined.

Most obstetricians rely on uterine fundal height, fetal abdominal circumference (AC) measurements and sonographic estimate of fetal weight for the detection of fetuses at risk for intrauterine growth restriction (IUGR) or for macrosomia. Both low birth weight and excessive fetal weight at delivery are associated with an increased risk of newborn complications during labor and the puerperium. The perinatal complications associated with low birth weight are most often attributable to fetal prematurity, but may sometimes also arise as the result of intrauterine growth restriction. For macrosomic fetuses or those with birthweight > 4000 grams, potential complications associated with delivery include shoulder dystocia, brachial plexus injuries, bony injuries and intrapartum asphyxia, as well as maternal risks that include birth canal injuries, pelvic floor injuries and postpartum hemorrhage. Macrosomic babies are often born of diabetic mothers, and thus are also at risk for metabolic disorders postnatally.¹

Fetal size is usually categorized on the basis of estimated fetal weight being small (<10th percentile, SGA), appropriate (10th-90th percentile, AGA), or large (>90th percentile, LGA) for gestational age. Antenatally, several biometric parameters have been used to estimate fetal size, IUGR and macrosomia. These would include biparietal diameter, head...
circumference, abdominal circumference and femur length. However, fetal size has not been found to accurately identify those fetuses at nutritional risk.² Fat content correlates directly with energy stores. Fat mass and lean body mass are often used in the nutritional assessment of the individual. Fat constitutes 12%–14% of birth weight and has been shown to account for 46% of the variation noted in neonatal weight.³ Consequently, ultrasound-generated estimates of fetal fat may be useful in the evaluation of fetal growth abnormalities. Larciprete, el al.⁴ found, in a case control study, that SCTT was reduced in infants with IUGR compared with controls, indicating that specific changes in fetal body composition occurs in fetuses with chronic metabolic impairment. On the other hand, Tantanasis, et al.⁵ measured fat thickness at three different points on the fetal body: the biparietal diameter, the abdominal circumference and the thoracic spine, and found the values of the three variables were significantly higher in those whose mothers who had high GTT compared to those whose mothers had normal GTT.

The aim of this study was to determine if fetal abdominal subcutaneous tissue thickness (FASTT) is significantly correlated with biometric measurements and with age appropriate weight categories, and whether it can predict the mode of delivery in a sample population of Filipino fetuses.

**Objectives**

**General**

To determine the correlation of fetal abdominal subcutaneous tissue thickness of Filipino fetuses at term with other biometric measurements and with neonatal outcome.

**Specific**

To determine the relationship of fetal abdominal subcutaneous tissue thickness at term with sonographic fetal measurements such as BPD, HC, AC and SEFW by Hadlock.

To determine the association of fetal abdominal subcutaneous tissue thickness at term and appropriateness for age of sonographic fetal weight (SGA, AGA, LGA) and actual birth weight.

To determine the accuracy parameters of fetal abdominal subcutaneous tissue thickness cutoff value as determined by ROC curve in this study to predict mode of delivery in terms of sensitivity, specificity, positive and negative predictive values.

To determine the intrarater reliability of different sonologists measuring FASTT using Intraclass correlation coefficient.

**MATERIALS AND METHODS**

**Study Design**

This is a prospective, correlational study of 150 gravid women at term gestation (≥ 37-39 weeks gestation) within one week of delivery at the Department of Obstetrics and Gynecology. Included in this study were term singleton pregnancies coming in at the Section of Ultrasound and Perinatology for pelvic ultrasound and fetal biometry who eventually delivered within a week in the same institution. Excluded were those who delivered more than a week from the last fetal biometry or growth measurements and those with fetal congenital anomalies.

**Sample Size**

A sample of 150 subjects were included based on the following assumptions:

a. Correlation coefficient desired is 0.85
b. 95% confidence level to be significant.

Eligible subjects were enrolled in the study consecutively after informed consent and data base forms were filled up. Menstrual age was calculated from the given first day of the last menstrual period confirmed by either a first-trimester or an early second-trimester ultrasound. Maternal age, gravidity, menstrual age at time of scan and presence of maternal complications were documented.

All participants were scanned by board-certified obstetrician-sonologists at the Section of Ultrasound and Perinatology. Two-dimensional sonography using the GE Logic 200 3.5 to 5.0 MHz curvilinear pelvic probe were used to scan the fetuses. Standard fetal biometric parameters such as biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC) and femoral length (FL) were measured prospectively. Fetal weights were estimated...
using three-parameter (BPD, AC and FL) model as described by Hadlock and co-workers.

The thickness of the subcutaneous fat tissue at the anterior abdominal wall was measured. The transverse section of the fetal trunk at the level of the abdominal circumference was obtained with fetal abdomen free from contact with arms or legs, with amniotic fluid between the fetal trunk and the uterine wall. Once this section was acquired, a magnification of the anterior abdominal wall was obtained. Subcutaneous fetal fat tissue was recognized as an external hyperechoic surface. The thickness of this layer was measured by placing one caliper exactly between the amniotic fluid and the fetal skin and the other caliper exactly between the subcutaneous fat layer and the anterior side of the liver in contact with the anterior abdominal wall. Thickness was measured three times by the same sonologist on duty.

Neonatal outcomes such as age of gestation at delivery, mode of delivery, birthweight and appropriateness for age of gestations such as small or large for gestation were recorded.

Each pregnancy was treated as a separate data unit. Data management and encoding were facilitated using Microsoft Excel. Intrarater reliability was determined using Intraclass correlation coefficient. Correlations of fetal abdominal tissue thickness with outcomes such as fetal BPD, HC, AC and SEFW and neonatal outcome as actual birth weight were done using Pearson’s correlation coefficient and linear regression. T-test was also used to determine association between continuous variables. ROC analysis was also done to determine the cutoff value of FASTT and accuracy parameters. For all tests, a 95% confidence level was considered significant.

**RESULTS**

Table 1 shows the characteristics of patients. All are AGA except for 6 subjects LGA, and majority were born by NSD. Mean sonographically estimated fetal weight (SEFW) was 3047 grams, and lower mean actual birth weight was 3157.7 grams. Mean BPD was 89.9 cm, head circumference was 317.9 and abdominal circumference was 330.7 cm.

Intrarater reliability using intraclass correlation (ICC) showed a correlation coefficient of 0.81, a high coefficient indicating very good agreement among the three measurements of FASTT done on each subject. This means that subcutaneous abdominal fat can be measured reliably with ultrasound.

<table>
<thead>
<tr>
<th>Table 1. Profile of patients.</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age for Weight</td>
<td></td>
</tr>
<tr>
<td>AGA</td>
<td>144</td>
</tr>
<tr>
<td>LGA</td>
<td>6</td>
</tr>
<tr>
<td>Mode of Delivery</td>
<td></td>
</tr>
<tr>
<td>NSD</td>
<td>110</td>
</tr>
<tr>
<td>CS</td>
<td>40</td>
</tr>
<tr>
<td>SEFW, in grams</td>
<td></td>
</tr>
<tr>
<td>Mean +/-SD</td>
<td>3047.3 +/-.304.8</td>
</tr>
<tr>
<td>Median</td>
<td>3039</td>
</tr>
<tr>
<td>Range</td>
<td>2230-3830</td>
</tr>
<tr>
<td>Actual Birth Weight</td>
<td></td>
</tr>
<tr>
<td>Mean +/-SD</td>
<td>3157.7 +/-233.5</td>
</tr>
<tr>
<td>Median</td>
<td>3203</td>
</tr>
<tr>
<td>Range</td>
<td>2650 - 3770</td>
</tr>
<tr>
<td>Biparietal Diameter</td>
<td></td>
</tr>
<tr>
<td>Mean +/-SD</td>
<td>89.9 +/-5.47</td>
</tr>
<tr>
<td>Median</td>
<td>90</td>
</tr>
<tr>
<td>Range</td>
<td>66.7 - 98</td>
</tr>
<tr>
<td>Head Circumference</td>
<td></td>
</tr>
<tr>
<td>Mean +/-SD</td>
<td>317.9 +/-49.7</td>
</tr>
<tr>
<td>Median</td>
<td>326</td>
</tr>
<tr>
<td>Range</td>
<td>307 - 344</td>
</tr>
<tr>
<td>Abdominal Circumference</td>
<td></td>
</tr>
<tr>
<td>Mean +/-SD</td>
<td>330.7 +/-14.6</td>
</tr>
<tr>
<td>Median</td>
<td>333</td>
</tr>
<tr>
<td>Range</td>
<td>289.9 - 371</td>
</tr>
</tbody>
</table>

For all subjects, STT ranged from 0.76 mm to 8.16 mm. Actual birth weight ranged from 2650 to 3770 grams, and classified according to weight for age would include only AGAs and LGAs. Thus we did not have any subject classified as SGA, nor did we have any macrosomic subjects.

Table 2 shows the results of correlation analysis of STT (average of three measurements) with some biometric parameters.

From the table, it can be seen that three fetal measurements showed significant correlation with STT, namely AC (Figure 1), Estimated Fetal Weight (Figure 2) and actual BW (Figure 3). STT accounted for 10.2% of the variations in AC, 7.7% in EFW and 6.4% in actual birthweight. BPD and HC did not show significant correlation with STT. STT showed higher correlation with AC than with EFW and actual BW.
Table 2. Correlation of fetal biometric measurements with subcutaneous abdominal fat thickness.

<table>
<thead>
<tr>
<th></th>
<th>BPD</th>
<th>AC</th>
<th>HC</th>
<th>EFW</th>
<th>Actual BW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correlation Coefficient (R)</td>
<td>0.013</td>
<td>0.329</td>
<td>0.048</td>
<td>0.289</td>
<td>0.266</td>
</tr>
<tr>
<td>P value</td>
<td>0.976</td>
<td>0.000</td>
<td>0.560</td>
<td>0.000</td>
<td>0.001</td>
</tr>
<tr>
<td>Coefficient of Determination</td>
<td>0.00</td>
<td>10.2</td>
<td>0.00</td>
<td>7.7</td>
<td>6.4</td>
</tr>
</tbody>
</table>

Table 3 shows the association of STT with weight for age and mode of delivery. Mean subcutaneous abdominal fat was significantly thicker in LGA than AGA babies. On the other hand, subcutaneous abdominal fat was significantly less thick in those delivered by CS than those delivered by NSD.

Table 3A shows the 2 x 2 frequency table of subjects who underwent CS and NSD based on a cutoff measure of ≤5.4 mm STT. The cut off value was determined using ROC analysis.

Table 4A shows that 19 out of 40 subjects who underwent CS had an STT of ≤5.4 mm, for a sensitivity of 47.5%. This means that using ≤5.4 mm STT, we can identify or predict correctly those who would undergo CS less than half of the time. On the other hand, we can correctly predict in 82.7% of the time that those with an STT of >5.4 mm (but not greater than 8.16 mm which is the highest value in our dataset), would have an NSD delivery. With a cutoff of ≤5.4 mm, STT was not very accurate in predicting CS deliveries, but is highly accurate in predicting NSD deliveries.

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In terms of diagnostic yield or the proportion who underwent CS who had a fetal STT of ≤5.4 mm and those who delivered by NSD who had >5.4 mm fetal STT, the values obtained were very nearly...
similar with those for sensitivity and specificity. Positive Predictive Value (PPV) was 50%, meaning among those with STT of ≤5.4 mm, 50% underwent CS. Negative Predictive Value (NPV) was 81.2%, meaning those with fetal STT of >5.4 mm, 81% had NSD delivery. Diagnostic yield is low for CS and high for NSD. For our particular dataset, CS was associated with smaller values of STT, NSD with higher values regardless of the indication for CS.

| Table 4A. | STT against manner of delivery based on cut off ≤5.4mm |
|---|---|---|
| | CS | NSD | Total |
| ≤5.4*mm | 19 | 19 | 38 |
| >5.4 mm | 21 | 91 | 112 |
| Total | 40 | 110 | 150 |

*Based on ROC analysis which selects the cutoff point that shows the best combination of sensitivity and specificity.

| Table 4B. | Accuracy parameters for STT at a cutoff of ≤5.4mm. |
|---|---|---|---|---|
| | Sensitivity | Specificity | Positive Predictive Value | Negative Predictive Value |
| Mode of delivery (NSD, CS) | | | | |
| Cutoff | 47.50% | 82.7% | 50% | 81.2% |
| ≤5.4mm | (31.5-63.9) | (74.3-89.3) | (33.2-66.8) | (72.8-88.0) |

**DISCUSSION**

Fetal size alone, as measured by the various biometric parameters measured with ultrasound device, may not be sufficient to identify nutritionally at risk fetuses. Studies have shown that babies identified initially as SGA, specifically those termed as symmetric SGAs, may be well nourished, and therefore not nutritionally at risk. On the other hand, babies classified as AGAs were found to be nutritionally at risk, in some studies. There were also LGAs who were found to be at par with AGAs as far as risk for adverse outcomes were concerned. Thus, there was a need to supplement the current parameters in identifying those fetuses at risk antenatally, and one of these may be the use of Subcutaneous Fat Tissue Thickness, which can be measured at different sites, but most commonly measured on the abdomen. Fat content correlates directly with energy stores. Fat mass and lean body mass are often used in the nutritional assessment of the individual. Fat constitutes 12%–14% of birth weight and has been shown to account for 46% of the variation noted in neonatal weight. Consequently, ultrasound-generated estimates of fetal fat may be useful in the evaluation of fetal growth abnormalities.

A study by Witoon Prasertcharoensuk and Parat Bunlengsanoh showed highly significant correlation of abdominal fat thickness with birthweight. Fetuses with STT ≤4 mm were found to be more likely to have low birth weight. The diagnostic performance of this method was: a sensitivity of 90.0% (95%CI=86.8-93.3), a specificity of 53.5% (95% CI=48.1-58.9), a positive predictive value of 5.7% (95% CI=3.2-8.3) and negative predictive value of 99.4% (95% CI=98.6-100.0). The authors concluded that sonographic measurement of the fetal abdominal fat thickness less than or equal to 4mm may be useful for screening of low birth weight infants. Rigano, et al. found that abdominal circumference in fetuses from mothers with and without gestational diabetes was similar, but there was a difference in the fetal fat tissue thickness at the time of diagnosis, suggesting that metabolic or nutritional status may not be accurately diagnosed with biometric parameters, thus a need for measurement of subcutaneous fat thickness antenatally. Gardeil, et al. found that infants with subcutaneous fat less than 5 mm at 38 weeks (n = 51) were almost five times more likely to have a birthweight below the 10th centile than those with subcutaneous fat of 5mm or more (n = 75). The incidence of neonatal morbidity was also significantly higher in infants with subcutaneous fat less than 5mm, compared with those with subcutaneous fat of 5mm or more (20% versus 8%, P < .05). Decreased subcutaneous fat was also associated with a high prevalence of low ponderal index, regardless of birth weight category. The authors concluded that measurement of fat in the abdominal wall is a simple technique with sensitivity for predicting low birthweight similar to that of conventional sonography and might potentially predict fetal growth restriction irrespective of fetal weight.

This study presents evidence of highly significant correlation between STT and abdominal
circumference, SEFW and actual birthweight, but not with BPD and HC. Highest correlation was with AC, and this may be due to the fact that subcutaneous fat is a component of the structures measured by AC. AC is measured at the widest point in the abdomen, through the liver at the level of the left portal vein or stomach. AC is determined not only by growing tissues (mainly liver) but also nutrient storage in the form of subcutaneous fat and liver glycogen. It can be significantly decreased in nutritional growth restriction and increased in diabetic macrosomia where elevated blood glucose levels lead to increased metabolic storage. Assimakopoulos, et al. (2007) showed that FASTT was positively correlated with birthweight (Pearson’s, r = 0.784, P < 0.001). Assimakopoulos, et al. (2007) showed that FASTT was positively correlated with birthweight (Pearson’s, r = 0.784, P < 0.001). Assimakopoulos, et al. (2007) showed that FASTT was positively correlated with birthweight (Pearson’s, r = 0.784, P < 0.001).

The relationship between fetal size and subcutaneous fat thickness was also found to be significant in this study, but our results are only limited to the relationship between AGA and LGA, with STT. We found that STT was significantly thicker in LGAs compared to AGAs (7.42mm vs. 6.23mm, P=0.0001). We did not have any case of SGA. This may due to the fact that SGAs are overrepresented in premature babies and the study is confined only to term pregnancies. Assimakopoulos, et al. found that fetuses with low FASTT were also more likely to be delivered through normal vaginal delivery (7.8 ± 0.1 mm), while higher FASTT was correlated with operative vaginal delivery (7.9 ± 0.2 mm) and cesarean section (8.6 ± 0.3 mm) (ANOVA, P = 0.034). With increasing FASTT, the likelihood of operative vaginal and cesarean delivery increased.

In the present study, we also found that STT was a predictor of mode of delivery, but results are not expected: those delivered by CS had lower fat thickness than those delivered by NSD (5.91 mm vs. 6.61 mm, P=0.031). Decisions on mode of delivery usually do not depend only on fetal size. Even large babies, unless they are macrosomic, can be delivered by NSD, whereas AGAs can be delivered by CS, if some problems are noted prior to delivery. A maternal decision to have elective CS is another factor affecting mode of delivery. A plausible explanation is that problems concerning the well being of some AGA fetuses were probably detected, especially those with very thin subcutaneous fat (we had measurements of 0.76mm, 1.56mm to 4mm) and may have undergone CS for these reasons. One limitation of this study is that we did not include specific indications for CS, which should be included in future studies, to correlate results better especially since not all sections are done merely because of large babies or contracted pelvic measurements. The relatively large number of AGAs who underwent CS resulted in low values for STT for CS deliveries which were not offset by the higher STT values of LGAs who also underwent CS. Notable though, is the observation that there were only six LGA babies and that all of them were delivered by CS, a reflection of a small sample size of LGAs represented in this study. Using our data set, sensitivity of STT to predict CS was low, while specificity or ability to rule out CS was high. Thus for our study, the probability that those with STT ≤5.4 mm will not undergo CS is 81% while the probability that those with STT ≤5.4 mm will undergo CS is only 50%.

This study found significant association of FASTT with abdominal circumference (Figure 3), SEFW (Figure 4) and actual birth weight (Figure 5) among Filipino fetuses, similar to the findings done by several authors on fetuses mainly of Caucasian race. We also found significant correlation of fetal size with FASTT, with large fetuses showing thicker FASTT than smaller fetuses. However, this study was not able to show a direct relationship of FASTT with mode of delivery, specifically, its ability to predict CS. This may be due to factors not considered in this study, as well as the small sample size of LGAs relative to AGAs.

**CONCLUSION**

The measurement of STT can be accurately measured sonographically and is a good parameter for estimation of fetal size, with thicker STT associated with larger fetal size but may not be able to predict accurately CS deliveries since not all sections are done due to feto-pelvic disproportion. Measurement of FASTT may be more useful, however, to aid in the assessment of fetal nutritional risk, intrauterine growth restriction or macrosomia.

**RECOMMENDATIONS**

For future studies, sufficient numbers of SGAs and LGAs or a wider range of birthweights should be included in the study to improve power to establish significant difference or improve accuracy testing. Indications for mode of delivery should be considered to better explain relationship between mode of delivery and fetal size.
REFERENCES

Comparative Study of 24-Hour Postoperative Hemoglobin on Manual Extraction Versus Spontaneous Placental Delivery Among Emergency Low Segment Transverse Cesarean Section Delivered Patients from March to August 2010

Objective: To determine if manual removal of placenta is associated with significant blood loss 24H postoperative versus spontaneous delivery of placenta among women delivered by Low Segment Transverse Cesarean Section (LSTCS).

Study Design: Experimental Study Design

Participants: Consenting house case patients for LSTCS

Main Outcome: Hemoglobin difference 24H postoperative

Methods: A randomized study of 87 patients with normal pregnancies undergoing emergency LSTCS. Patients were randomly assigned to manual group (n = 46) and spontaneous group (n = 41).

Results: 24H post op, there was a drop in hemoglobin level in both groups, 1.551±(0.882)gm/dL in the manual group and 1.342±(0.733)gm/dL in the spontaneous group. The decrease in mean hemoglobin levels between the 2 groups is not statistically significant having a P-value of 0.595 which is greater that the chosen level of significance, P=0.05.

Conclusion: Therefore, manual delivery of placenta is not associated with greater risk of blood loss compared to spontaneous delivery of placenta. Manual removal of placenta is not associated with significant greater risk of blood loss 24 hours post-op compared to spontaneous delivery.

Key words: spontaneous delivery of placenta, manual removal of placenta

Cesarean delivery is now the most commonly performed surgical procedure in obstetrics. At term, the uterus is perfused at a rate of 450-650mL/min and this increase in blood flow contributes to a blood loss of approximately 1000mL. Obstetric hemorrhage accounts for one of the major complications of cesarean section with reported hemorrhage rate varying between 4.3-8%. Baksu (2005) mentioned that postoperative mortality rate is influenced by operative blood loss during cesarean section.

Safety of cesarean delivery has improved since the techniques have become more routine and it is relatively associated with low maternal mortality rate. Moreover, surgical techniques have been studied to reduce the risk of operative blood loss of cesarean section. Such techniques include finger splitting versus cutting of incision, in situ stitching versus exterioration and stitching of uterus and mode of placental delivery.

Mode of placental delivery has been a subject of discussion for the past decades. Apparently, surgeons have different opinions on the best technique of placental delivery. Morales, et al. stated that manual cleavage remained the standard technique for placental delivery in many institutions while several studies recommended spontaneous delivery of placenta in cesarean sections. Thus, the researchers wish to find out if manual delivery of placenta is associated with significant blood loss at the time of operation.
General Objective

To determine if manual removal of placenta is associated with significant blood loss 24-hour post-op versus spontaneous delivery of placenta among women delivered by LSTCS in Negros Oriental Provincial Hospital.

Specific Objectives

1. To describe the demographic data of patients (maternal age, parity, birthweight, gestational age, indication for c-section)
2. To measure the 24-hour post-op hemoglobin level of women with manual extraction of placenta.
3. To measure the 24-hour post-op hemoglobin level of women with spontaneous delivery of the placenta.
4. To compare the difference of 24-hour post op hemoglobin level of manual extraction vs. spontaneous delivery and determine if there is a statistical difference.

Review of Related Literature

The two methods of placental delivery are spontaneous and manual removal. Published studies had conflicting results on the best mode of placental delivery with regard to blood loss during cesarean delivery.

A study done by McCurdy and Magann, et al. showed less blood loss in patients with spontaneous expulsion of placenta. Blood loss was directly measured intraoperatively in which mean blood volume loss were 927ml and 666ml for spontaneous and manual group, respectively. Chandra, et al. however, used 24-hour post-op hemoglobin to reflect blood loss and the change in hemoglobin (-1.81g/dL, manual; -1.72 g/dL, spontaneous) was similar for both groups.

Consequently, Gol, et al. conducted a randomized study of 200 women with normal pregnancies who had cesarean section. Blood loss was measured using a volume and gravimetric method. Postoperative hemoglobin levels were measured at 24H and 48H. Mean intraoperative blood loss of manual delivery of placenta (626±253mL) was not different from spontaneous separation group (589 ± 272mL). There was a decrease in postoperative hemoglobin in both groups but not significantly different.

In F. Hached University Teaching Hospital in Tunisia, Hidar, et al. conducted a randomized study on 302 women who underwent elective or emergency cesarean section as to the effect of placental removal method on perioperative hemorrhage. Hematocrit and hemoglobin were measured between 24-48H after operation. The mean drop in hematocrit was greater in manual removal group than in spontaneous group.

Since morbidity rate is influenced by postcesarean endometritis and mortality rate by operative blood loss, Baksu, et al. made a study on 840 women who underwent cesarean section in Training and Research Hospital, Istanbul, Turkey. The site of uterine repair and method of placental removal were included in the study. The study showed a decrease in 48H postoperative hemoglobin and hematocrit was significantly greater in the manual group regardless of the site of uterine repair than the spontaneous group.

In two trials conducted in Iran and Switzerland, significant blood loss was measured as >2gm/dL of hemoglobin at 72H postop. Included were all women who underwent elective or emergency cesarean section and whose uteri were repaired in situ. The studies showed spontaneous delivery of placenta reduces significant blood loss compared to manual removal of placenta.

Ramadani conducted a randomized study of 400 women who underwent primary or repeat, whether elective or emergency in King Abdulaziz University Hospital in Jeddah, Saudi Arabia. The 72H postoperative hemoglobin was decreased in both manual removal group (9.0±1.2g/dL) and spontaneous delivery group (9.9±1.2g/dL) and was statistically significant (P= 0.006).

In the Philippines, a study done by Que-Villarin and Sulay at the Cebu Doctors University Hospital in Cebu showed postoperatively (72H) a drop in hematocrit of 3.47±1.60 volume percent in spontaneous group and 4.26±1.87 volume percent in the manual group (P=0.0003).

Locally, there has been no study on the method of placental delivery during cesarean section and operative blood loss. In our setting, manual removal of placenta has been commonly practiced as well as 24H postop hemoglobin determination to assess
blood loss. Its safety and efficacy have not been studied.

MATERIALS AND METHODS

Study Design: Experimental Study Design

Study Population: Consenting patients for emergency LSTCS with no complications

Exclusion Criteria:

- Patients with no consent
- Multiple gestation
- Medical co-morbidity such as DM, gravidocardiia
- Hypertensive disorders of pregnancy
- Hemorrhagic disorders of pregnancy
- Repeat LSTCS with adhesions
- Intraoperative uterine atony
- Clotting disorders
- Ruptured BOW with fever

All patients with consent upon admission were included in the study. Patient assignment to spontaneous group or manual group was done using labeled cards in sealed envelope.

Maneuvers

This randomized controlled trial was conducted at the Negros Oriental Provincial Hospital from March 2010 to August 2010. Excluded in the study were women who refused to participate, those with abnormal placentation, clotting disorders, multiple gestation, ruptured BOW with fever, history of postpartum hemorrhage, pregnancy induced hypertension and repeat CS with adhesions and those with intra-operative uterine atony and pregnancy with AOG <36 weeks. Pre-operative CBC was taken on admission. Low segment transverse cesarean section as described by Atkinson\(^1\) was done by a senior resident and junior resident under spinal anesthesia.

After delivery of the baby, incisional angles were clamped accordingly. The spontaneous group contained women in which the resident waited till the placenta delivered spontaneously. Controlled gentle cord traction was performed (if needed) to help placental delivery. On the other hand, the manual group, the placenta was cleaved out manually as soon as the baby was delivered.

Methylergometrin one ampule was given intramuscularly, as soon as the cord was clamped and cut; and 20 units oxytocin was incorporated in 1000ml D5LR and infused. Moreover, uterine massage was also done to effect adequate uterine contraction. Abdominal pack was used to wipe the uterus to remove blood clots and possible retained placental tissue in both groups. The uterus was sutured in situ. All patients received prophylactic antibiotic before operation. Ice pack was applied on the hypogastrium post-op.

Twenty four hours post-op, CBC was taken for determination of post-op hemoglobin. The difference in blood loss was taken to be the difference between pre-op and post-op hemoglobin.

Data Analysis

In determining the level of hemoglobin level of each study group, central tendency called Mean was computed, expressing quantitative data as mean±SD. T-test for independent samples was used to determine whether a significant difference exists between the level of hemoglobin of manual and spontaneous group.

Mann Whitney test was required if normality of population where the samples were taken was not met like the comparison of mean difference of hemoglobin for each indication of cesarean section.

RESULTS

Eighty seven subjects qualified for this study, 41 for the spontaneous group and 46 for the manual group. Seventy seven percent were delivered by primary low segment transverse cesarean section and 22.7% by repeat low segment transverse cesarean section under spinal anesthesia.

The indications for C-section include malpresentation, non-reassuring fetal heart rate, previous C-section and dystocia. Malpresentation was the most common indication for C-section with a rate 36.36% for both groups, followed by dystocia (28.41%), previous CS (22.73%) and non-reassuring FHR (12.5%).

Table1 shows the demographic data of participants in the 2 groups with regards to age, parity, age of gestations and fetal weight. The mean age (years) of patients was 27.217±(6.373) and 28.±(6.544) for manual and spontaneous, respectively.
Most frequent age of patients in the study was 24 for spontaneous and 25 for manual. The number of pregnancies (parity) has a mean of 1.891±(1.120) for the manual group and 1.786±(1.025) for the spontaneous group. Most of the participants have a parity of 1. Frequent gestational age of each group was 39 weeks for manual and spontaneous groups, and mean of 39.087±(1.1208) and 39.095±(1.008), respectively. Neonates for the manually delivered placenta had birthweights frequently at 3000gms and 2900gms for the spontaneously delivered placenta. Mean birth weights were 2977.174 ± (335.297) gms and 2992.857±(362.339) gms, respectively.

In both groups, most of the subjects had hemoglobin loss of 0.40-1.15g/dL and 1.16-1.91g/dL. Thirty one patients (35.63%) had hemoglobin loss of 0.40-1.15g/dL and 31 subjects (35.63%) had hemoglobin loss of 1.61-1.91g/dL. Moreover, 13 (14.63%) subjects had hemoglobin loss of 1.92-2.67g/dL followed by 7 subjects (9.7%) with <0.40g/dL. Only 5 subjects had hemoglobin loss above 2.68g/dL.

Table 2 shows the mean hemoglobin for each indication of cesarean section. Differences of each indication between the groups were not statistically significant (P>0.05).

The mean levels of pre-op hemoglobin in both group were almost the same, 11.989±(1.037)g/dL for manual and 12.112±(0.87)g/dL for spontaneous. A decrease in post-op hemoglobin is observed in both groups with a mean of 10.329±(1.104)g/dL for manually delivered placenta and 10.573±(1.069) g/dL for spontaneous group. The mean difference of hemoglobin of the 2 groups, 1.551±(0.882)g/dL for manual and 1.342±(0.733)g/dL for spontaneous has a P value of 0.595. (Table 3)

**DISCUSSION**

Several studies showed that manual delivery of placenta is more associated with significant blood loss compared to spontaneous. Some trials though showed no significant difference between the two methods. Several methods of determining blood loss were used in the previous studies, gravimetric or volumetric. In this study, 24H postop hemoglobin was used for convenience and is accurate enough to measure intraoperative blood loss. With this, both groups showed a decrease in hemoglobin 24 hours post-op, however the mean difference between pre-op and post-op hemoglobin is not statistically significant with a P value of 0.619. The result means that manual removal of placenta is not associated with significant blood loss 24 hours post-op.

Previous studies have shown higher operative blood loss and lower postop hemoglobin levels in patients who had manual removal of placenta. As explained by McCurdy, et al. shearing of the placenta before significant involution of placental bed may result in unaltered perfusion and increase in blood loss. Moreover, Berghella, et al. mentioned that many investigators hypothesized that blood loss is increased in manual removal because dilated
sinuses in the uterine wall are not closed yet. However in this study, manual removal of placenta is not associated with significant blood loss and is supported by the study of Go, et al. This is most likely because myometrial contractility and retraction to compress the blood vessels are the main factors for achieving hemostasis at the placental site. Moreover, the clamping of the incisional angles and use of oxytocin are important factors in preventing excessive blood loss. The type of uterine incision is also an important factor in determining the amount of blood loss during cesarean section. A lower uterine incision has less effect on operative blood loss compared with lower vertical or classical incisions. Previous studies done by McCurdy, et al., Magann, et al. and Hached, et al. (2003) used low vertical and classical incisions in a number of patients which could result in increased operative blood loss. On the other hand, recent studies showing increased operative blood loss on manual removal of placenta used 72H post-op hemoglobin to measure blood loss which can be subject to other variables beyond 24H post-op, like uterine atony and subinvolution. Uterine massage which can also hasten uterine contraction and decrease intraoperative blood loss was not done by Sulay, et al. (2006) but was done in this study.

**CONCLUSION**

Consequently, there is no significant difference in the amount of average blood loss 24H post op between manual and spontaneous delivery of placenta. Manual removal is not associated with greater risk of operative blood loss 24hours post-op compared to allowing spontaneous delivery of the placenta. Both methods of placental delivery are safe and effective.

To minimize compounding variables that may affect the result, elective cesarean delivery can be done as well as direct measurement of blood loss intraoperatively. Moreover, in emergency cesarean section, the number of hours the patient is in labor can be quantified to determine if there's a bearing on the possible result since this was not done in this study.

**REFERENCES**

A Randomized Trial of Carbetocin versus Oxytocin in the Prevention of Postpartum Hemorrhage in Cesarean Section

ROSALE M. TORRES, MD; CARMELA MADRIGAL-DY, MD, FPOGS AND MA. CLARA LDL. OZAETA, MD, FPOGS

Department of Obstetrics and Gynecology, Dr. Victor R. Potenciano Medical Center

Objective: This is a single blinded, randomized controlled trial on women with singleton term pregnancy delivered by cesarean section to compare the efficacy of a single intravenous injection of carbetocin with a standard 8-hour intravenous infusion of oxytocin.

Methods: The trial was conducted in the delivery unit of a tertiary hospital from January 1, 2011 to June 30, 2011. Sixty two patients were randomized to receive either a single injection of carbetocin or an 8-hour infusion of oxytocin. Outcome measures were intraoperative blood loss, uterine tonicity and need for uterotonic intervention.

Results: The mean estimated blood loss with carbetocin was significantly less with a P value of < 0.01 (483.87 ml). Intravenous injection of 100mcg of carbetocin-produced tetanic uterine contractions within 3 minutes, lasting for about 5 minutes, followed by rhythmic contractions for a further 50 ± 20 minutes. Need for uterotic intervention was clinically indicated in two (6.45%) of the women given carbetocin compared to 12 (38.71%) of the women given IV oxytocin infusion. Adverse effects of the treatments were not significantly different between the two groups.

Conclusion: Carbetocin was superior to oxytocin in the outcome parameters measured. Estimated blood loss and the need for additional uterotonic agents were lower in the carbetocin group. Uterine tone and early involution of the uterus is likewise better in the carbetocin group.

Key words: postpartum hemorrhage, carbetocin, oxytocin, cesarean section

woman. Faced with the morbidity and mortality brought about by postpartum hemorrhage research studies are crucial in decreasing its incidence. Common tools on which we count are the improvement of monitoring, the definition of strategies based on standardized protocols and a prophylactic treatment having an effective constrictive action on the uterus.

Oxytocin is the most common uterotonic drug used to prevent and treat postpartum hemorrhage in North America. However, there are limitations to its use. Oxytocin has a very short duration of action, requiring continuous infusion to achieve sustained uterotoninc activity, a long-acting oxytocin analog, 1-deamino-1-monocarba-(2-O-methyltyrosine)-oxytocin d (COMT), carbetocin, lasts 4 to 7 times longer than oxytocin, with a similar side effect profile, greater efficacy rate and prolonged pharmacological effects, is used in preventing postpartum hemorrhage after a cesarean delivery. It is less likely to induce hypertension and has a low incidence of adverse effect. So, it should be considered as a good alternative to conventional uterotonic agents used in managing the third stage of labor.

Several clinical trials have compared carbetocin with oxytocin. One trial cites the use of carbetocin resulted in a statistically significant reduction in the need for therapeutic uterotonic agent [relative risk (RR) 0.44, 95% confidence interval (CI) 0.25 to 0.78] compared to oxytocin for those who underwent cesarean section, but not for vaginal delivery. Carbetocin is also associated with a reduced need for uterine massage in both cesarean and vaginal deliveries (RR 0.38, 95% CI 0.18 to 0.80; RR 0.70, 95% CI 0.51 to 0.94) respectively. However, this outcome measure was only documented in one study on cesarean delivery and in the only study on vaginal delivery. Pooled data from the trials did not reveal any statistically significant difference in terms of the adverse effects between carbetocin and oxytocin.

In the clinical study by Dansereau (1999), that overall oxytocic intervention rate was 7.4%. The odds of treatment failure requiring oxytocic intervention was 2.03 (95% confidence interval 1.1 to 2.8) times higher in the oxytocin group compared with the carbetocin group, respectively, 32 of 318 (10.1%) versus 15 of 317 (4.7%), P < .05. Carbetocin, a new drug for the prevention of uterine atony, appears to be more effective than a continuous infusion of oxytocin and has a similar safety profile.

The patients included in the study were randomized using computer generated random numbers in the data analysis function of excel version 8.0. The patients were divided in two groups and were blinded as to the medications given. Study group A received single intravenous injection of 100mcg carbetocin and group B received eight hours infusion of oxytocin. Upon admission, vital signs were gathered and logged on the case record form. All patients were enrolled for the study after informed consent. The study was approved by the Ethics Committee of the tertiary hospital. All patients included in the study had a baseline complete blood count (CBC) and a repeat after 24 hours.

Thirty one women received 100mcg carbetocin IV immediately after placental delivery while 31 women received 10 U oxytocin IV infusion. The effect of a single 100 mcg IV dose of carbetocin with that of a standard 8-hour 10 international units (IU) IV infusion of oxytocin was noted based on the following parameters: 1) Intraoperative blood loss, measured from the time of drug administration up to skin closure. Estimation of blood loss by OR staff using a gravimetric method is accurate and applicable by weighing surgical sponges used for blood collection and a visual estimate of the blood by the anesthesiologist by measuring the volume of the suctioned blood, 2) Assessment of uterine tone, made after placental delivery, immediately after drug administration, 30 minutes after drug administration, during skin closure and 1-2 hours in the recovery room. Uterine tone was measured by palpation of the fundus on the basis of the following criteria: Firm-when gentle finger pressure depressed the uterus slightly and transiently; Hard- a non depressible, tetanic uterus and Softer/Boggy- a soft, atonic uterus, 3) An additional uterotonic agent was used for a boggy uterus noted 1-2 hours in the recovery room. Vital signs were assessed within 24 hours after the operation. Signs and symptoms of adverse events in the operating room were noted.

CONCLUSION

With a single IV injection of carbetocin, results greater than those on oxytocin with regards to the maintenance of uterine tonicity and the limitation of blood losses in the peri and postoperative period, during a delivery by cesarean section. Carbetocin is effective with its long half-life, on a single injection, whereas oxytocin requires repeated injections or a
perfusion of several hours, with a variability of the administered doses.

By its long duration of action and its simpleness of use, carbetocin makes possible the standardization of procedures, unanimously felt today as indispensible. It favors the production of simple, reproducible and applicable protocols in all centers, in order to improve the prevention of postpartum hemorrhage and its complications.

Carbetocin works well in the preventive strategy, and the current experience is sufficient. It is an interesting therapeutic alternative to oxytocin in the prevention of uterine atony after cesarean section.

REFERENCES

Combination Methods Using Fetal Abdominal Circumference and Maternal Characteristics in Predicting Term Fetal Birth Weight Among Low Risk Antenatal Population*

BELLA EMIKO B. CAÑIZARES, MD; ROSELYN C. YU, MD AND RAYMOND S. SULAY, MD, FPOGS

Department of Obstetrics and Gynecology, Perpetual Succour Hospital, Cebu City

**Objective:** To compare combination methods using third trimester ultrasound measurements of abdominal circumference (AC) with maternal characteristics in predicting term fetal birth weight among low risk antenatal population.

**Design:** Prospective comparative study.

**Setting:** The study was carried out at the Department of Obstetrics and Gynecology at a tertiary hospital between October 2010 to May 2011.

**Subjects:** This study was performed among 135 low risk term pregnancies that were delivered at a tertiary hospital from October 2010 to May 2011.

**Data Collection Procedures:** All measurements from maternal characteristics and ultrasonographic fetal AC were determined and gathered from the study subjects. Using these variables, two equations were developed and the accuracy of predicting the actual BW was established and compared.

**Results:** The predicted fetal weight using equation 1 was 9.5% higher than the actual weight compared to equation 2, which was 3,177.31(298.46) slightly higher by 99.942(355.41) from the actual fetal weight of 3,077.37(369.41) (P=0.001). The predicted fetal weight using equation 2 was 3.1% higher than the actual fetal weight value. When prospectively validated, equation 2 had a significant and stronger correlation (r = 0.450, P = 0.000) with BW as compared to equation 1 (r = 0.029, P = 0.738). The results further validated that the regression model of equation 2 was a better predictor method and had lesser error in predicting BW as compared with equation 1.

**Conclusion:** The equation for predicting fetal BW using maternal characteristics alone was more accurate than the formula using combination of fetal AC and maternal characteristics. Therefore, maternal characteristic estimation is recommended to yield a better prediction and to further evaluate fetal well being.

**Key words:** abdominal circumference, maternal characteristics, birth weight, term

A ccurate estimation of fetal weight is one of the important and principal factors in the management of labor and delivery. During the last decade, estimated fetal weight has been part of standard antepartum evaluation of high-risk pregnancies and deliveries. It is hoped that early recognition of an abnormality coupled with appropriate surveillance and intervention will optimize perinatal outcomes.

Ultrasound has been used since the mid-1960s as a tool for determining fetal size. Many investigators have created models to estimate birth weight utilizing different ultrasound measurements in many combinations. Fetal abdominal measurements, mostly abdominal circumference (AC), are not only included in the majority of commonly used weight equations, but also have the greatest impact on weight estimation.

New and theoretically defensible equations that prospectively predict fetal birth weights from maternal and pregnancy-specific characteristics have been

developed. The predictive efficacy of 59 scientifically justifiable terms were evaluated simultaneously to eliminate any confounding co-variation and to determine which predictors could independently account for variations in birth weight. Aside from maternal race, 7 maternal and pregnancy-specific variables were independently important in predicting birth weight for otherwise healthy pregnant women.

It has been suggested that accurate estimation of fetal weight would help in successful management of labor and care of the newborn in the neonatal period. It helps avoid complications associated with fetal macrosomia in high birth weight babies, thereby decreasing perinatal morbidity and mortality.

It is therefore valuable to determine the most accurate method of fetal weight estimation in our local setting and consequently improving the management of maternal conditions and preventing poor fetal outcome.

Review of Related Literature

It has long been established that birth weight is a major determinant of infant mortality in the first year of life. Mortality rates are known to be affected by extreme birth weights more than gestational age. Hence there is more importance attached to antenatal birth weight determination.

Accurate prediction of fetal weight has been of great interest in obstetrics. As fetal weight cannot be measured directly, it must be estimated from fetal and maternal characteristics. Many workers have used different methods to achieve this. Of the various methods, the most commonly used are the clinical and ultrasonographic methods. Only a few studies have compared the accuracy of fetal weight by clinical and ultrasonic measurements.

Various factors have been associated with alterations in fetal growth. These include genetic factors such as neonatal sex and ethnic group; geographic factors such as altitude; maternal factors such as pre-gravid height, weight and weight gain during gestation; and to a lesser degree, paternal factors such as height and weight.

In previous studies, no standardized method was used for clinical estimation, making it subjective, poorly defined and non-reproducible. The sonographic method is widely used because it is objective, reproducible and involves a well-defined measurement procedure. Fetal size is most commonly characterized by comparison of ultrasonographically estimated fetal anthropometric parameters. The most sensitive of the individual fetal parameters for the detection of growth abnormalities is the abdominal circumference. A study conducted by Nahum, et al. showed that of the four standard fetal biometric dimensions, the correlation between the fetal abdominal circumference and term birth weight was by far the best. This suggests that the fetal abdominal circumference is the most predictive of the standard fetal ultrasonographic measurements for estimation of term birth weight. More than 20 years ago, Ogata et al, by serial ultrasound examinations, reported an association in diabetic mothers of an abnormally large fetal abdominal circumference between 28-32 weeks' gestation with accelerated fetal somatic growth.

On the other hand, a study conducted by Shittu, et al. on the standardized method of clinical estimation of birth weight had been found to correlate well with actual birthweight.

By using birth-weight prediction equations based on parental and pregnancy-specific characteristics alone, fetal weight at and near term can be predicted with a high degree of accuracy (± 7.6%-8.4%). In healthy pregnant women, this approach is at least as reliable as clinical palpation and ultrasonographic fetal biometry. However, in predicting fetal macrosomia, neither palpation nor ultrasonographic fetal biometry was known to be used with any degree of certainty.

Maternal characteristics that influence birth weight include pre-pregnancy weight or maternal body mass index, weight gain in pregnancy and maternal height, which are all indicators of maternal nutritional status. This quantitative assessment of maternal characteristics serves to objectively quantify clinical variables that have been used in clinical assessments and are thought to be predictive of fetal weight.

It has been well recognized that fetuses at the extremes of the normal birth weight range are associated with increases in perinatal morbidity, mortality and adverse developmental outcomes. In addition, macrosomic infants have a 6-fold increase of marked birth trauma. The antenatal fetal weight measurement is of tremendous importance because it can give a useful information for the fetal growth assessment. This information could help us decide the time of delivery, the need for specific obstetrical intervention, and whether it is necessary for the delivery to be at a center equipped with intensive neonatal care support.
As a result of recent improvements in the accuracy of fetal-weight predictions, practicing obstetricians can now undertake prospective interventions more confidently than before, with the aim of minimizing intrapartum and peripartum risks for both fetuses and mothers.

Significance of the Study

Over the past decades, countless researches have been conducted to improve prediction of fetal weight. Ultrasound assessment has become the standard practice of most obstetricians in monitoring and identifying fetal biometric measurements and well being but there is still no conventional method of accurately predicting fetal outcome.

This study aimed to determine the most accurate way of measuring fetal weight. This study can aid the general practitioners, specialists in Obstetrics and Gynecology, residents and fellows in training and physicians whose practice is centered on the care of women.

Objectives

General Objective

To make a comparative estimation of fetal weight using combination methods of third trimester ultrasound measurements of abdominal circumference (AC) and maternal characteristics in the prediction of term birth weight among low risk antenatal population.

Specific Objectives

1. To determine the patients profile in terms of age and parity.

2. To determine the distribution and typical indicators of patients' profiles as variables in predicting fetal weight by using equations 1 and 2.

3. To determine mean differences between predicted and actual fetal weight in equations 1 and 2.

4. To compare the accuracy of using equations 1 and 2 in predicting fetal weight and actual fetal weight using correlation coefficient.

Scope and Limitation

Scope

The data were gathered and determined from measurements of all maternal characteristics and ultrasound measurement of fetal abdominal circumference in 135 singleton pregnant women. Two equations that were based on these measurements were used and analyzed to predict birth weight.

Limitation

The study was only limited to pregnant mothers who were enrolled in the Maternity Service Package at Perpetual Succour Hospital, Cebu City. The study was also limited to pregnancies with all live-born singleton babies and mothers that fit in the inclusion criteria. Several technical limitations of the sonographic technique include limited visualization of fetal structure due to fetal position, anterior placentation and maternal obesity.

MATERIALS AND METHODS

Study Design

This is a prospective comparative study.

Study Setting

The study was carried out at the Obstetrics and Gynecology Department of a tertiary hospital between October 2010 to May 2011. The study protocol was approved by the Department and written informed consent was obtained from each subject before participating in this study.

Study Subjects

The study subjects were 191 mothers with singleton pregnancy in the 2nd and 3rd trimesters that were enrolled and had routine prenatal check-up under the Out Patient Department Maternity Service Package and all delivered at this hospital. Only 135 study subjects fulfilled the inclusion criteria.

Inclusion Criteria

Patients included in the study were as follows: singleton term pregnancies (37 to 42 weeks), reliable
date of last menstrual period, abdominal circumference measured within 11 weeks of delivery. Gestational age was established based on 1) a history of regular menses, with interval between 25 and 31 days with a confirmatory obstetric ultrasonographic examination between 14 and 20 weeks, or 2) a first trimester dating obstetric ultrasonographic examination.

**Exclusion Criteria**

Patients excluded in the study were as follows: those whose pregnancies could not be accurately dated; women with preterm (<37 weeks) or postterm pregnancies (>42 weeks), multiple gestations, preexisting or coexisting medical illnesses (e.g., hypertension, diabetes mellitus, cardiac and thyroid problems), uterine anomalies as well as fetal anomalies, as these factors may independently affect fetal growth.

**Data Collection**

Two-dimensional Ultrasonographic Measurements

The ultrasound examination for abdominal circumference was evaluated and performed within 11 weeks of delivery. Only one trained OB sonographer performed the ultrasound measurement.

Maternal Data

Maternal anthropometric data included height, weight at 26 weeks age of gestation (kg), weight gain rate during the third trimester (total weight gain in kg divided by days of gestation), maternal hemoglobin concentration during the third trimester (g/dl), age and parity.

**Equation**

Recently, a new theoretically-defensible equation that can predict individual birth-weight prospectively from maternal characteristics was developed. To do this, the efficacy of 59 scientifically justifiable terms was evaluated simultaneously, obviating any confounding co-variation and determining which of the predictions could account for variation in birth-weight that others could not. Aside from maternal race, only seven maternal and pregnancy specific variables were important in the prediction of birth-weight for otherwise normal gravidas. By using these routinely recorded variables, an equation based on maternal and pregnancy-related characteristics alone was developed to predict birth weight based on the following factors: maternal height, maternal weight at 26 weeks’ gestation, maternal weight gain rate during the third trimester, maternal hemoglobin concentration during the third trimester, parity, fetal sex, and gestational age at delivery.

Estimation of fetal weight was determined by comparing two formulas. First equation required data regarding maternal characteristics which were collected and added, and were applied within the formula:

The first equation is as follows:

Birth weight in grams = -1627 + (13.18 x fetal AC) + (16.23 x delta US) + [0.00009966 x gestational age in days x maternal height in centimeters x maternal weight at 26 weeks in kilograms] + [3.173 x gestational age in days x maternal third trimester weight-gain rate in kilograms per day) x (parity + 1)],

Where : AC = fetal abdominal circumference

delta US = elapsed time in days between the acquisition of ultrasonographic fetal biometric measurements and delivery date

Maternal weight gain rate = Weight gain in kilograms per day from 28 weeks age of gestation to delivery, and

gestational age = days since the onset of the last normal menses, which equals the conception age (days) + 14.9

This was a formula described by Nahum, et al. and used since 2007.

The second equation is as follows:

Birth weight (grams)= -3044+ gestational age (days) x [(23.6+(0.243 x fetal sex)) + [0.000281 x maternal height (cm) x maternal weight at 26 weeks (kg)] + [3.11 x maternal weight gain rate (kg/day) x (parity +1)] - (0.318 x maternal hemoglobin concentration in grams per deciliter)].
where: fetal sex =-1 for females;+1 for males;0 for unknown gender gestational age=conceptual age (days)+14.10

The formula described was obtained from other previously published algorithms and found more accurate than all others derived from either maternal characteristics or fetal ultrasonographic data according to the study conducted by Nahum, et al. on Caucasian gravidas.10

After delivery, the resident pediatrician weighed the newborn babies within 30mins of delivery employing a standard analogic scale corrected for zero error. All of the data needed to complete the equation were collected and tabulated.

Correlation between the actual birth weight with the sonographic and maternal characteristics were collected and computed independently after the delivery. The resulting equation of the stepwise analysis, which included the significant variables, was used to calculate the projected birth weight. The calculated birth weight was then compared with the actual birth weight at delivery. All calculations were single handedly computed by the researcher.

**Data Processing**

This study utilized the frequency and percentage distribution to present the profiles of patients, which were categorical. On the other hand, fetal weights and other clinical results were indicated through mean and standard deviation. As for the test of mean difference between actual and estimated fetal weights, paired t-test was used. The test of correlation employed Pearson r Product Moment Correlation Coefficient. Lastly, the inference was tested at 0.05 level of significance.

**RESULTS**

Fifty seven percent out of 135 patients had ages between 24 to 30 years old. Twenty six percent of patients were aged 31 to 38 years old, and 17% were within the 17 to 23 years old range. The patients’ average age was 27.59 years old. On the other hand, 51% had G1P0 parity, 24% had G2P1, 10% had G3P2, and 6% had G2P0.

Out of 135 patients, 54% were males while 46% were females. The patients’ maternal profile were as follows: mean height of 152.64(5.85), mean weight of 58.69(9.06), mean age of gestation of

274.64(7.42), and mean weight gain rate of 8%(5.0).

Lastly, using clinical assessment, the results showed a fetal weight of 297.62(204.48), delta US of 46.41(21.64), and Hemoglobin (Hgb) mean of 12.05(1.98). These were variables utilized in equations 1 and 2 as predictors of fetal weight. (Table 1)

<table>
<thead>
<tr>
<th>Variables for Equation(s) in Estimating Fetal Weight</th>
<th>No. of Patients</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fetal Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>62</td>
<td>46</td>
</tr>
<tr>
<td>Male</td>
<td>73</td>
<td>54</td>
</tr>
<tr>
<td>Maternal Profile</td>
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<tr>
<td>Height (mean,sd):cm</td>
<td>152.64 (5.85)</td>
<td></td>
</tr>
<tr>
<td>Weight (mean,sd):kg</td>
<td>58.69 (9.06)</td>
<td></td>
</tr>
<tr>
<td>AOG (mean,sd)</td>
<td>274.64 (7.42)</td>
<td></td>
</tr>
<tr>
<td>Weight gain (mean,sd):rate</td>
<td>8% (5.0)</td>
<td></td>
</tr>
<tr>
<td>Clinical Assessment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fetal AC (mean,sd)</td>
<td>297.62 (204.48)</td>
<td></td>
</tr>
<tr>
<td>Delta US (mean,sd)</td>
<td>46.41 (21.64)</td>
<td></td>
</tr>
<tr>
<td>Hgb (mean,sd)</td>
<td>12.05 (1.98)</td>
<td></td>
</tr>
</tbody>
</table>

Utilizing equation 1, the predicted fetal weight was 3,401.65(2,701.49), which was off by a difference of 324.28(2,715.96) from the actual fetal weight (P=0.168). Equation 1’s predicted fetal weight was 9.5% higher than the actual weight. On the other hand, equation 2’s predicted fetal weight was 3,177.31(298.46) slightly higher by 99.942(355.41) from the actual fetal weight of 3,077.37(369.41) (P=0.001). In effect, equation 2’s prediction was 3.1% higher than the actual fetal weight value. In comparison, equation 2 had lesser error in predicting actual fetal weight than equation 1. (Table 2)

| Equation 2 proved to be better predictor of actual fetal weight as revealed in the strength of correlation (r = 0.450, P = 0.000) as compared to equation 1 (r = 0.029, P = 0.738). The result further validate that the regression model of equation 2 is a better predictor method as compared with equation 1. |

**DISCUSSION**

Evidence has shown how lifelong well-being strongly depends on intrauterine growth and
development during intrauterine life. Fetal growth can achieve its full potential only with an adequate and fine-tuned interaction between mother, placenta and fetus. Several environmental and maternal factors may alter this delicate equilibrium. Application of such an individually adjustable standard for fetal growth allows better distinction between normal and abnormal smallness. Since the metabolic environment in utero has great impact on growth and development postnataally, it is important to recognize these abnormalities antenatally.

For many decades, the estimation of fetal weight has been integrated into the standard routine antepartum evaluation of high-risk pregnancies and deliveries. The accuracy of predicting fetal weight is vital in the management not only during pregnancy but also during labor and delivery. There have been numerous researches done and equations formulated so as to come up with the most accurate method of predicting fetal birth weight but not one has mastered such prediction. In the Philippines, no studies have been conducted comparing ultrasound and maternal characteristics in predicting fetal weight.

Obstetric sonographic assessment for the purpose of obtaining fetal biometric measurements to predict fetal weight has been integrated into the mainstream of obstetric practice in the past quarter century. From its inception, this method has been presumed to be more accurate than clinical methods for estimating fetal weight. The reasons for this assumption vary, but the fundamental underlying presumption is that sonographic measurements of multiple linear and planar dimensions of the fetus provide sufficient parametric information to allow for accurate algorithmic reconstruction of the 3-dimensional fetal volume of varying tissue density. As such, the ultrasonographic technique represents the newest and most technologically sophisticated method of estimating fetal weight. The accuracy of the fetal weight predictions generated by ultrasound equations depends on a wide variety of factors. Modern algorithms that incorporate standardly defined fetal measurements (eg, some combination of fetal AC, FL, BPD and HC) are generally comparable in their overall accuracy in predicting fetal weight. Surprisingly, the study conducted by Nahum, et al. showed that fetal abdominal circumference (AC) proved to be as accurate as the other classes of equations based on multiple standard ultrasonographic fetal measurements. Of the four standard fetal biometric dimensions, the correlation between the fetal AC and term birth weight was by far the best for all four measurements, which suggests that the fetal AC is the most predictive of the standard fetal ultrasonographic measurements with regards to estimation of fetal weight. The abnormal fetal growth pattern becomes apparent after 26-28 weeks of gestation, when it is confined to the abdominal circumference and subcutaneous fat.

New and theoretically defensible equations to prospectively predict individual birth weight from maternal and pregnancy-specific characteristics have been developed. Aside from maternal race, 7 maternal and pregnancy-specific variables were independently important in predicting birth weight for otherwise healthy pregnant women. These prospectively measurable variables account for more than 36% of the variance in term birth weight and can be used to accurately predict fetal weight to within 267g-288g (± 7.6%-8.4%) of individual birth weights. In addition, 68%-75% of newborn weights can be estimated to within ± 10% of the actual birth weights.

### Table 2. Paired t-test of mean differences between predicted and actual fetal weight.

<table>
<thead>
<tr>
<th>Fetal Weight Prediction Model(s)</th>
<th>Indicator(s) mean</th>
<th>sd</th>
<th>Paired t-test Difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Equations 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predicte weight</td>
<td>3,401.65</td>
<td>2,701.49</td>
<td>324.283 (2,715.96)</td>
<td>0.168NS</td>
</tr>
<tr>
<td>Actual weight</td>
<td>3,077.37</td>
<td>369.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equation 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predicted weight</td>
<td>3,177.31</td>
<td>298.46</td>
<td>99.942 (355.41)</td>
<td>0.001s</td>
</tr>
<tr>
<td>Actual weight</td>
<td>3,077.37</td>
<td>369.41</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
by using this method. Prospective use of this maternal-characteristics equation yields a correlation of 0.59 between predicted and actual birth weights, with a mean absolute prediction error of 275 ± 229g (8.0% ± 7.1 of actual birth weight). In 86% of cases, the birth weight predictions were accurate to within ± 15%, and in 70% of cases, they were accurate to within ± 10% of actual birth weight. The accuracy of this new method was recently tested by an independent group of investigators from the Czech Republic. It was confirmed that its accuracy was comparable to that of the widely-used ultrasound-alone method of estimation within the normal birth weight range.1

The above findings have important implications for developing countries like ours where there is lack of technologically advanced ultrasound machines capable of sophisticated functions such as fetal weight. This study implies that maternal characteristics alone, without the aid of ultrasound, can accurately predict fetal outcome and prevent fetal and maternal complications in areas here in the Philippines wherein ultrasound is not easily obtainable. With the availability of laboratory, even a midwife or nurse can readily compute for the fetal weight.

The timely detection of growth failure is important because of its ever-more apparent links to perinatal morbidity and mortality as well as adverse

Endogenous and extrinsic factors influence fetal weight. These encompass maternal factors (eg, race, stature, genetics), paternal factors (eg, paternal height), environmental influences (eg, altitude, availability of adequate nutrition, degree of physical activity), physiologic factors (eg, altered glucose metabolism, hemoglobin concentration, microvascular integrity), pathologic factors (eg, hypertension, uterine malformations), and complications of pregnancy (eg, gestational diabetes mellitus, preeclampsia). After gestational age and maternal race, several other major parental, environmental and pregnancy-specific determinants of birth weight are relevant for mothers with otherwise uncomplicated pregnancies. These include the following: 1) maternal height, 2) maternal obesity, 3) maternal pregnancy weight gain, 4) parity, 5) fetal sex, 6) ambient altitude, 7) maternal hemoglobin concentration. Taken together, these measurable factors can explain more than two fifths of the variance in term birth weight. As evidently shown in Table 4, Equation 2 proved to be a better predictor of actual fetal weight as revealed in the strength of correlation as compared to equation 1. The result further validated that equation 2 is a better predictor method of fetal birth weight as compared with equation 1. No studies have shown that maternal characteristics alone is superior to ultrasound in predicting fetal weight in low risk population. A prospective study conducted by Shittu, et al. showed that clinical estimation of fetal weight is as accurate as the ultrasonographic method of estimation within the normal birth weight range.

The results are encouraging. With the maternal characteristics only assessed, equation 2 resulted in a significant improvement in the prediction of fetal weight over equation 1. Between the two equations, the second formula using the maternal characteristics alone had the lowest mean errors.

CONCLUSION

The above findings have important implications for developing countries like ours where there is lack of technologically advanced ultrasound machines capable of sophisticated functions such as fetal weight. This study implies that maternal characteristics alone, without the aid of ultrasound, can accurately predict fetal outcome and prevent fetal and maternal complications in areas here in the Philippines wherein ultrasound is not easily obtainable. With the availability of laboratory, even a midwife or nurse can readily compute for the fetal weight.

The timely detection of growth failure is important because of its ever-more apparent links to perinatal morbidity and mortality as well as adverse
effects in childhood and later life. Improvements in neonatal care and better surveillance methods of the at-risk fetus place emphasis on better screening and detection of antenatal growth problems. Fetal biometry continues to have an important role, and its most effective use in the third trimester is its provision of an estimated fetal weight which, plotted on customized charts, will give an indication of the growth status of the fetus.

RECOMMENDATIONS

Further studies are recommended in improving the accuracy of fetal weight in high-risk patients (hypertensive, diabetic) to give the appropriate management and improve fetal outcome. Other equations for prediction of fetal weight should be explored to give way for more tailored specific needs, such as accurate prediction of low birth weight as well as identification of macrosomic infants. Supplementary research can also be conducted concerning analysis of the equation, like what maternal characteristics greatly influence the accuracy of its prediction.

REFERENCES

Herlyn-Werner-Wunderlich Syndrome: Report of Two Cases

MA. CORAZON A. ISIDTO, MD  AND  NAILANI Z. TAN, MD, FPOGS

Department of Obstetrics and Gynecology, Negros Oriental Provincial Hospital, Dumaguete City

Uterine didelphys with obstructed hemivagina and ipsilateral renal agenesis is a rare congenital anomaly referred to as Herlyn-Werner-Wunderlich (HWW) syndrome first described in 1922. The incidence and cause are not known. This paper aimed to 1) present two cases of the syndrome presenting at different periods of a woman's life, and 2) discuss the diagnosis and management of HWW. The first case of HWW presented a year after menarche as abdominal mass and pain with mullerian anomaly seen on the right side. The second case presented in early adult life with less severe symptoms of abdominal pain and mass, with mullerian anomaly seen on the left and associated with perforation of the obstructed left hemivagina to the right vagina.

Key words: obstructed hemivagina, Ipsilateral renal agenesis

When a young woman presents with abdominal pain and abdominal mass, correct diagnosis of this rare condition of HWW is necessary to prevent unnecessary invasive intervention such as exploratory laparotomy and hysterectomy. This paper presents two cases of HWW, presenting in early post menarche and early adult life, with different degrees of severity of symptoms, the first case affecting the right side of the mullerian system and ipsilateral kidney and the second case, with less severe symptoms, affecting the left side of the mullerian system, and associated with perforation of the obstructed left hemivagina to the normal right vagina.

Case 1

C.S., 12 years of age; menarche at 11 years old, was admitted for severe right lower quadrant pain. Condition started 4 months prior to admission (a year after menarche) as a gradually enlarging mass palpated by the patient at the right lower quadrant of the abdomen, associated with increasing pain during each menstrual period. One week prior to admission, she consulted at the Out-patient surgical department. Patient was afebrile. Physical examination revealed a slightly tender cystic mass at the right lower quadrant, measuring 7.0cm x 7.0cm x 10.5cm. Rectal examination revealed the mass to be anterior and to the right of the rectum. Abdominal ultrasound revealed cystic mass at the right lower quadrant with low level echoes. Ultrasound of the kidneys revealed absence of the right kidney with slightly enlarged left kidney. CT scan of the abdomen showed the cystic mass at the right iliac, with absence of the right kidney. She was eventually admitted for increasing abdominal pain, and was referred to the Ob-Gyn Department, with the impression of ovarian cyst. She underwent combined transvaginal and abdominal ultrasound which showed uterine didelphys with right-sided hematometrocolpos (Figure 1). Vagina on the left side was separated from the right hemivagina by a blind vertical septum measuring 5.0mm in thickness. She was then scheduled for marsupialization of the vaginal septum under general anesthesia. Chocolate brown mucoid discharge was suctioned from the obstructed right hemivagina. Postoperative course was uneventful and she was discharged after 3 days.
Case 2

B.R., 24 years of age, with menarche at 14 years old, G0, sexually active, was admitted for abdominal mass associated with on and off lower abdominal pain, severe dysmenorrhea and dyspareunia under the surgery department. Abdominal ultrasound done revealed a cystic mass with carpet of low to medium level echoes at the left iliac area, measuring 9.0cm x 10.0cm x 9.0cm. Left ovarian cyst was entertained and she was referred to the Obstetrics and Gynecology Department. Internal examination during menstruation revealed bulging mass at the left side of the vagina extending to the lower third of the vagina. An opening was seen at the left lateral fornix just lateral to the cervix, with dark brown blood exiting from the small opening. 3D transvaginal sonogram was done which showed uterine didelphys with left-sided hematocolpos and left hematocervix. (Figures 2 & 3).

Incidental finding of bilateral polycystic ovaries was seen, with failure to elicit a sliding organ sign suggestive of pelvic adhesions, possibly secondary to endometriosis. Intravenous pyelography done revealed absence of the left kidney. She was given cyproterone acetate-containing pills taken continuously for three months to treat the bilateral polycystic ovaries and possible existence of pelvic endometriosis. Repeat transvaginal sonogram three months after revealed resolution of the left hematocolpos and improvement of symptoms of dysmenorrhea. She was then admitted and underwent wide excision of the perforated vaginal septum, with marsupialization and drainage of the left-sided hematocolpos.

DISCUSSION

Maldevelopment of the Mullerian duct system can result in various uterine, vaginal and renal abnormalities. Obstructed unilateral vagina in patients with uterus didelphys is frequently associated with ipsilateral renal agenesis known as the Herlyn-Werner-Wunderlich syndrome.1 Lately, this is classified under the new term Obstructed Hemivagina Ipsilateral Renal Anomaly (OHVIRA) syndrome to include other anomalies of the uterus associated with renal agenesis like septate uterus.2
Incidence

The incidence and cause of HWW syndrome are not known.1,3 Related to this syndrome, the incidence of uterus didelphys is about 1/2000 to 1/28000, accompanied by unilateral renal agenesis in 43% of cases.4 The incidence of unilateral renal agenesis is 1/1,100 and 25%-50% of affected women have associated genital abnormalities.5 A report showed that the incidence of an obstructive mullerian anomaly is 0.1% - 3.8%.6 It has been concluded that there is a close relationship between female genital and urogenital anomalies.

In the Philippines, the Pediatric Gynecology Unit of Philippine Children's Medical Center diagnosed 5 cases in its 5 years of existence. One case was reported at St. Luke's Medical Center in 2011.14 In our locality, these are the only two cases reported for the past 20 years.

Etiology and Pathophysiology

Embryologically, the inner genital organ and the lower urogenital system are formed from the development of two pairs of Wolffian ducts (mesonephric duct) and Mullerian ducts (paramesonephric duct) in each gender. In the female, the paramesonephric ducts grow down close to the central line beside the mesonephric ducts and they meet across the mesonephric ducts. The paramesonephric ducts meet to form the uterovaginal canal and the uterus, oviducts, and upper two thirds of the vagina develop from it.1 However, in the early 4th week of gestation, the mesonephric ducts and ureteral bud are affected in some unknown way to develop a malformation and genetic mutation, thus leading to unilateral developmental abnormalities of the mesonephric duct; the ureteral bud can be the cause of unilateral vaginal obstruction and ipsilateral renal agenesis.1,5 In other words, abnormalities of the mesonephric duct cause the ipsilateral paramesonephric duct to deviate laterally. The abnormal mesonephric duct prohibits crossing of the opposite paramesonephric duct and fusion, resulting in uterus didelphys. Vaginal obstruction develops because the paramesonephric ducts cannot meet the urogenital sinus centrally. Without a mesonephric duct, the ipsilateral kidney and ureter can not develop, consequently HWW syndrome occurs. In the two cases presented, the first case, the unilateral renal agenesis developed on the right side, which is more common.7 The cause for this right side predilection is uncertain, but the right side of the rat embryo is reportedly more susceptible to hypoxic damage than the left side. This could be due to a precocious mitochondrial maturity on the left side of the embryo, resulting in high energy reserves and less tissue damage following hypoxia.8 In the second case of HWW, the renal agenesis developed on the left, which is less frequent than the right sided renal anomaly.

Signs and Symptoms

The syndrome usually presents with progressive and recurrent pelvic pain after the menarche, as in the first case presented. It is not initially diagnosed because of the regular flow from the unobstructed vagina, as in the two cases presented which were initially admitted and seen under the surgical department. Sometime after menarche (one year after menarche in the first case), the retention of menstrual blood in the obstructed hemivagina leads to the formation of hematocolpos, which is usually clinically detected as a pelvic mass. Diagnosis may be further delayed, if a communication between the two vaginas exist1, as in the second case presented, which presented 10 years after menarche, with less severity of symptoms. Not only a dilated hemivagina but also a dilated uterine cavity (hematometrocolpos) was present in the first case. In delayed cases, bleeding into the peritoneal space may occur as a consequence of retrograde menstruation. Endometriosis can also be formed in these patients,6,9,10 as in the second case presented.

Diagnosis

Ultrasound (abdominal with transvaginal, 2D or 3D) can usually diagnose the presence of uterine anomaly and hematocolpos. Other methods for diagnosis, include computed tomography, magnetic resonance imaging, hysterosalpingography and exploratory laparoscopy. MRI is the most effective method.11 It can delineate well the uterine contour, the shape of the intrauterine cavity and the cervix, which cannot be well delineated using the ultrasound and CT scan. In the presence of a possible endometriosis, pelvic inflammation and adhesions, as in the second case, MRI is less adequate as a diagnostic tool and the gold standard of diagnosis and treatment is laparoscopy.12
Treatment

Definitive treatment of HWW syndrome is resection of as much of the obstructing vaginal septum as possible. This rapidly relieves the symptoms and prevents complications related to cryptomenorrhea such as endometriosis, pelvic adhesions and infectious collections.\textsuperscript{1,10,12,13} There may be recurrence of the obstruction and pyometra after a simple incision only. Candiani, et al. have suggested marsupializing the vaginal margins after excision of the septum to allow ample drainage of the purulent material and better expose the cervix.\textsuperscript{6}

Prognosis

Fertility is preserved with this surgery, which is not significantly decreased in women with didelphic uterus.\textsuperscript{1} The outcomes of pregnancy reveal 87% go on to have successful pregnancy, while abortions occur in 23% of the patients, 15% have preterm births, and 62% have full term pregnancies and uncomplicated deliveries.\textsuperscript{3}

CONCLUSION

Early and accurate diagnosis of female reproductive tract disorders, including HWW syndrome, is necessary to prevent complications and preserve future fertility. In a woman presenting with cyclic pelvic pain and pelvic mass, especially close to menarche, the rare incidence of this syndrome, should be a consideration, especially in the presence of uterine didelphys. The urogenital system should be examined when a genital anomaly is identified and vice-versa. MRI is the most effective method and helps prevent unnecessary surgery. Due to its prohibitive cost, ultrasonography and computed tomography are most used instead. Treatment is wide excision of the obstructing vaginal septum and marsupialization to prevent further complications of infertility, endometriosis and pyocolpos. Since patient has only one kidney, prevention of urinary infection is very important.

REFERENCES

An Ovarian Sex Cord Tumor with Annular Tubules Presenting with Precocious Puberty

HELEN VALENZONA MADAMBA, MD and MA. CRISTINA PELAEZ-CRISOLIGO, MD, FPOGS

Department of Obstetrics and Gynecology, Philippine General Hospital, University of the Philippines Manila

The ovarian sex cord tumor with annular tubules (SCTAT) has a distinctive histologic appearance, composed of undifferentiated cells of sex cord derivation growing in the form of ring-like tubules. Case reports show that these tumors may present with precocious puberty and symptoms disappear with excision of the tumor. Concerns for this patient include not only the social stigma associated with the child being physically advanced for her age and the diminished ultimate height caused by the premature closure of epiphyseal growth centers, but as well as the risks of malignancy in a tumor whose malignant potential have yet to be studied.

The patient is a six-year old female who consulted due to vaginal bleeding, early breast and pubic hair development, and an abdominopelvic mass. Ultrasound showed a huge ovarian newgrowth with benign features. She underwent right salpingo-oophorectomy, and the specimen sent for histopathology revealed that the mass is made up of distinct concentric (annular) tubules randomly dispersed in the ovarian stroma. Histopathologic diagnosis was a sex cord tumor with annular tubules (SCTAT) of the right ovary.

It is imperative that in patients presenting with precocious puberty, an investigation for the specific cause be undertaken so that any hormone-secreting tumor may be removed. Management of these patients entails a multidisciplinary approach involving the gynecologist, pediatrician, endocrinologist and psychiatrist. Continuous monitoring of the patient is also indicated since any malignant behavior of individual tumors cannot be predicted.

Key words: precocious puberty, sex cord tumor with annular tubules
which combines features suggestive of a granulosa cell tumor with a pattern of growth reminiscent of Sertoli cells. Its morphologic hallmark is the presence of simple and complex annular tubules containing eosinophilic hyaline bodies, often calcified. It is distinct that up to 25% of these tumors are associated with the Peutz-Jeghers syndrome.

The aim of this report was to present a rare hormone-secreting ovarian tumor, the sex cord tumor with annular tubules presenting with the equally rare disorder of precocious pseudopuberty; the investigation of the possible causes of the symptoms and the approach to its diagnosis and management.

THE CASE

This is the case of G.M., a six year-old female from Binangonan, Rizal who consulted at our institution for vaginal bleeding. She has no history of pulmonary tuberculosis, bronchial asthma nor blood dyscrasias. She has no history of any surgical procedures or blood transfusion. The family history is non-contributory.

She was born vaginally to a 22 year-old G1P0 at home assisted by a midwife without any fetomaternal complications. She was breastfed for one and a half years, bottle-fed until 3 years old, given complementary feeding starting 5 months of age and presently has no food predilection. She received complete immunization for BCG, hepatitis B, diphtheria-pertussis-tetanus, oral polio vaccine and measles. Gross motor skills were at par with age. She walked at 1 year-old, had comprehensible speech at 3 years old, associative play at 3 years old, and cooperative play at 4 years old. She is presently in pre-school and is able to catch up with academic lessons.

History started one month prior to admission when the patient experienced vaginal bleeding consuming one pad, which resolved spontaneously. No medications were taken. No consult was done. One week prior to admission, vaginal bleeding recurred consuming 3-4 large diapers, prompting consult with a private physician. Ultrasound was done, which showed a right adnexal mass, probably ovarian in origin. One day prior to admission, the patient complained of vague abdominal pains with no other associated symptoms, hence consult at our institution.

At the Admitting Section, the patient was awake, ambulatory, oriented to time, place and person, cooperative, spoke spontaneously, intelligibly and with good eye contact. Cognitive functions were appropriate for age. The rest of the neurologic exam was essentially normal. The patient stood 124 cm and weighed 25 kg. Vital signs were stable. She had pink palpebral conjunctivae, anicteric sclera, no tonsillopharyngeal congestion, no nasoaural discharge, no cervical lymphadenopathies, no anterior neck mass. There were no gross chest deformities, but bilateral breast mounds were present with an areola 3cm in diameter (Tanner stage B3) (Figure 1). She had symmetric chest expansion, no retractions, with clear breath sounds, an adynamic precordium, no heaves nor thrills, with apex beat at the fourth left intercostal space, midclavicular line, with normal rate and regular rhythm, distinct heart sounds and no murmurs appreciated.

The abdomen was globularly enlarged with an abdominal girth of 61 cm. There were normoactive bowel sounds, no fluid wave appreciated, dull to percussion with no note of tenderness. There was a huge abdominopelvic mass reaching midway between the umbilicus and xiphoid process, which seemed predominantly cystic, slightly moveable and non-tender on deep palpation. There were fine axillary hairs on both axillae (Figure 2). There were no bone deformities. She had full and equal pulses, pink nail beds, no jaundice, no edema, no cyanosis. Over the mons pubis, there was minimal pubic hair (Tanner Stage P2) (Figure 3). She had normal external genitalia with note of minimal bleeding per vagina (Figure 4). On direct rectal examination, there was tight sphincteric tone, intact rectal vault with smooth mucosa and no nodularities. The posterior pole of the previously described abdominopelvic mass was palpable over the cul de sac area and seemed predominantly cystic and non-tender. There was no stool, nor blood per examining finger.

Admitting impression was a functional ovarian new growth, precocious puberty. A transrectal ultrasound was done, which showed a multiloculated, multiseptated anechoic cystic mass measuring 21.9cm x 18.2cm x 9.1cm with capsule and septum measuring 0.2cm each (Figure 5). Impression was that of an abdominopelvic mass to consider ovarian neogrowth probably benign by Sassone and Lerner with the uterine size compatible for a normal adult-sized uterus with thin endometrium. Bone aging based on the method of Greulich-Pyle, the patient’s left hand and wrist most closely resembled the standard for a 6-7 years, 10...
months old female. Complete blood count, blood chemistry and urinalysis showed results within normal range. The patient was scheduled for exploratory laparotomy and was managed preoperatively by a multidisciplinary team consisting of the Reproductive Endocrinology and Infertility Section, Gynecologic Oncology section, Pediatrics Service and the Child and Adolescent Psychiatry Service. She and her family were counselled regarding the effects of precocious pseudopuberty, the need for excision of the hormone-secreting tumor and the possibility of malignancy.

On the fifth hospital day, she underwent exploratory laparotomy with right salpingo-oophorectomy under general anesthesia. Intraoperatively, there was 50cc of pinkish ascitic fluid. The right ovary was converted to a 25cm x 22cm x 10cm cystic mass with smooth external capsule, which on cut section was multiseptated and multiloculated, containing clear serous fluid with no solid thickened areas and no papillary excrescences (Figures 6 & 7). The capsule and septum measured 0.2cm thick. The right fallopian tube was stretched out over the mass. The uterus was enlarged to six weeks size with smooth serosal surface. The left ovary and fallopian tube were grossly normal. There were no palpable pelvic lymph nodes. The three doughy and moveable para-aortic lymph nodes measuring 1.5cm x 1.5cm were not suspicious for malignancy and therefore not dissected. The rest of the abdominal and pelvic organs were grossly normal. The patient tolerated the procedure well. The rest of the hospital stay was unremarkable and she was discharged improved.

On follow up at the outpatient clinic after a week, there was a note of a decrease in the breast size with resolution of vaginal bleeding (Figure 8). Histopathology findings showed that the mass is made up of distinct concentric (annular) tubules randomly dispersed in the ovarian stroma (Figure 9). The individual tubules are lined by well-differentiated Sertoliiform cells with dense hyaline material in the lumens (Figure 10). The cells have pale cytoplasm and nuclei arranged antipodally around a hyaline body. This was signed out as a sex cord tumor with annular tubules (SCTAT), right ovary with no diagnostic abnormality recognized, right fallopian tube. The final diagnosis is precocious pseudopuberty secondary to a functional sex cord tumor with annular tubule formation (SCTAT), right ovary.

**DISCUSSION**

According to Garibaldi, et al. (2007), precocious puberty is defined as the onset of secondary sexual characteristics before 8 years of age in girls. Our patient presented with early growth spurt, fine axillary and pubic hair growth and vaginal bleeding. A study by Kalpowitz (2004) of 104 children revealed a low incidence of endocrine pathology and a high proportion of children with common benign variants of normal, hence most patients with minimal breast or pubic hair development and normal growth velocity can be evaluated with only a history, physical examination, and review of the growth chart, without a full endocrine evaluation. The incidence of this condition in the United States is estimated to be approximately 1 in 10,000 young girls.

An approach to diagnosis of patients with precocious puberty is to determine whether the cause is central or peripheral. Central precocity or true precocity entails GnRH dependence with an early maturation of the hypothalamic-pituitary-ovarian axis and hence, increase in the production of sexual hormones, causing symptoms of precocious puberty. As for peripheral precocity or precocious pseudopuberty, although there is increased production of estrogen, it is not dependent on GnRH production. It is not due to early maturation of the hypothalamic-pituitary-ovarian axis, but due to an exogenous production of estrogen, such as an adnexal or adrenal mass.

An etiologic diagnosis can frequently be made on the basis of clinical signs, bone age assessment, estradiol levels, GnRH stimulation testing and pelvic ultrasound examination. The causes of precocious puberty are broadly subdivided according to a functional classification based on gonadotropin dependence. True precocious puberty is dependent on gonadotropin and is always isosexual, the secondary sex characteristics develop appropriately for the genetic and phenotypic sex. It stems from hypothalamic-pituitary-gonadal activation. The gonadotropin-mediated increase in the size and activity of the gonads leads to increasing sex hormone secretion and progressive sexual maturation.

In precocious pseudopuberty, the sex characteristics may be isosexual or heterosexual. It is not dependent on the levels of gonadotropin. Isosexual conditions may be secondary to tumors secreting sex hormones or human chorionic
gonadotrophin, congenital disorders such as McCune-Albright Syndrome, congenital adrenal hyperplasia or hypothyroidism. On physical examination, there was note of an abdominopelvic mass, which on ultrasound revealed an ovarian new growth with benign features. With this finding, the hyperestrinism may be attributed to the functional ovarian new growth. Occasionally, there might also be heterosexual characteristics, where secondary characteristics occur in the patient of the opposite phenotypic and genetic gender. For example, when there is hirsutism and decreased pitch of voice in a female, or breast buds in a male.

**Sex Cord Tumor with Annular Tubules**

On histopathology, the ovarian new growth turned out to be a rare ovarian neoplasm, the sex cord tumor with annular tubular formation (SCTAT). In 1970, Scully introduced the term "Sex cord tumor with annular tubular formation" for a peculiar form of ovarian neoplasm which had a distinctive architecture. He described 13 tumors characterized by the formation of simple and complex rounded epithelial units appearing as ring-like tubules with a solid mass of cytoplasm at their centers; the peripheral nuclei wind around single or multiple hyaline bodies. The SCTAT lesion combines features suggestive of a granulosa cell tumor with a pattern of growth reminiscent of Sertoli cells. Its morphologic hallmark is the presence of simple and complex annular tubules containing eosinophilic hyaline bodies, often calcified. The ambiguous or biphasic nature of the tumor cells is also apparent on ultrastructural examination: features consistent with granulosa cell or non-specialized ovarian stroma, alternate with features indicative of Sertoli cell differentiation, notably the presence of Charcot-Bottcher filaments.

In the World Health Organization (WHO), SCTAT is placed in the category of unclassified sex cord-stromal neoplasms. However, it has a distinctive appearance that merits specific designation. The importance of segregating these tumors from others is also underscored by the finding that one third of cases were associated with the Peutz-Jeghers syndrome, a familial disorder characterized by an association of gastrointestinal polyps with melanin spots on the oral mucosa, lips and skin. Tumors associated with the Peutz-Jeghers syndrome are typically multifocal, bilateral, small (or even microscopic), calcified, and usually benign, although exceptions occur.

Nearly all women without Peutz-Jeghers syndrome present with a palpable mass. Our patient presented with precocious puberty and a huge abdominal mass, but did not show any evidence of pigmentation on the oral mucosa, lips or skin. Although extensive work up for Peutz-Jeghers syndrome was not done, there was no history of gastrointestinal symptoms to suggest presence of gastrointestinal polyps. Those unassociated with the Peutz-Jeghers syndrome are unilateral, often large, as seen in our patient. In the study by Young, et al. (1982), cysts up to 5cm in diameter were seen grossly in nine cases and two tumors were predominantly cystic. The tumors were oval to round and composed of firm nodular tissue usually described as yellow, yellow-tan, or pink-tan. In our patient, the right ovarian mass was huge, filling the abdominal cavity. It had a smooth external capsule and was multicystic, multisepated and multiloculated on cut section, containing clear serous fluid with no solid thickened areas, no papillary excrescences and no areas of hemorrhage and necrosis.

Patients with this tumor most commonly present in the third or fourth decade but the age ranges from 4-76 years. A number of SCTAT cases have been reported, including those by Hart, Kumar and Crissman, et al. (1980), Young, et al. (1982), Ahn, Chi and Lee, et al. (1986) and Torres. Symptoms of hyperestrinism have been described in approximately 50% of cases. Isosexual pseudoprecocity or other features of aberrant estrogen occurs in about 40% of cases, and occasionally, there are progesterone effects. In many patients with SCTAT, signs and symptoms of estrogenic hormonal influence or hyperestrinism are manifested. Abnormal vaginal bleeding and amenorrhea were observed in several patients. In our institution, only three cases of ovarian sex cord tumor with annular tubules including this case have been reported. Torres (1999) reported a similar case in a five-year old girl presenting as precocious puberty. She underwent exploratory laparotomy, right salpingooophorectomy, partial omentectomy and peritoneal fluid sampling. The histopathologic report showed "sex cord tumor with annular tubules, right ovary".

The tumors occurring in patients without the Peutz-Jeghers syndrome differed in their microscopic features from those associated with the syndrome. Those unassociated with Peutz-Jeghers syndrome...
commonly had foci in which cells differentiated in the direction of a granulosa cell tumor as evidenced by the formation of solid cellular islands devoid of an annular tubular architecture or in the direction of a Sertoli cell tumor as evidenced by an arrangement in the form of elongated tubules. According to the study by Young, et al. (1982) of 47 patients with SCTAT not associated with Peutz-Jeghers syndrome, masses were palpable on abdominal examination in 21 cases and on pelvic examination in 3 additional cases. Five of the 24 patients with masses complained of abdominal pain. Five girls had isosexual precocity and in three of them, the symptoms regressed after excision of the tumor. Unilateral salpingo-oophorectomy is the initial therapy of choice in young patients with a Stage 1A SCTAT who do not have the Peutz-Jeghers syndrome, because the rarity of involvement of the contralateral ovary. The possible role of complete surgical staging, chemotherapy and radiotherapy in clinically malignant cases needs further evaluation.

The prognosis for our patient is good, in that it acts as a benign mass, with regression of symptoms after excision of the mass. However up to 25% of SCTATs that occur in the absence of the Peutz-Jeghers syndrome have been clinically malignant. Metastatic potential of neoplasms resembling SCTAT have been reported to develop after postoperative intervals of 7.5 and 10.5 years. Tumors with infiltrative growth pattern and mitotic figures beyond the usual 3-4 per 10 high power fields are more likely to recur or otherwise behave aggressively. It is difficult, however, to predict the behavior of individual cases. It is therefore important for the patient to be regularly monitored for tumor recurrence and/or malignancy. The patient and the entire family should receive extensive counseling for the several changes in the patient: being physically and psychologically different from peers of her age, for possible short statural growth and the possibility of malignancy. With this patient, reassurance is given since almost immediately post-operatively, there was note of regression of the breast buds and cessation of menstrual bleeding.

CONCLUSION

Precocious puberty may affect a child’s psychosocial and emotional development, especially when she sees how different she is from her playmates. Stature may be a problem if without treatment due to the early closure of the epiphyseal plates. Diagnosis and treatment must be timely. Management of the patient should entail multidisciplinary approach involving the gynecologist, the pediatrician, the endocrinologist, and the psychiatrist.

More information regarding the natural course of rare ovarian newgrowths such as the SCTAT should be gathered so as to be able to adequately counsel the patient regarding possible recurrences of the mass, and worse, of the risk of malignancy.

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