Maternal Serum Alpha Fetoprotein Versus Ultrasound Criteria in Prediction of Outcome in Pregnancies with Suspected Morbid Adherence of the Placenta


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Abstract

Purpose: The study aimed at comparing unexplained elevated maternal serum AFP and ultrasound criteria in predicting the maternal outcome at delivery in patients with suspected morbid placental adherence.

Methods: The study was a prospective cohort study carried out at Ain Shams University Maternity Hospital. 60 pregnant women with suspected morbidly adherent placenta by transabdominal ultrasound had their maternal serum alpha-fetoprotein (MSAFP) levels measured. Women for other causes for MSAFP elevation were excluded. Statistical analysis was performed by chi-square test, Fisher’s exact test, Student’s t-test, and odds ratio calculation.

Results: In our study a sonographic score >3 was associated with morbid adherence at a sensitivity of 82.6%, specificity of 92.1%, positive predictive value [PPV] of 97.4%, negative predictive value [NPV] of 61.9%, positive likelihood ratio [LR+] of 11.6, and a negative likelihood ratio [LR–] of 0.2, while a MSAFP >2MOM was associated with morbid adherence of placenta at a sensitivity of 93.3%, specificity of 71.4%, PPV of 91.3%, NPV of 71.4%, LR+ of 3.2, and LR– of 0.1. Moreover we found that MSAFP >2MOM was associated with 3-fold, 7-fold, 2-fold, and 3-fold increase in intraoperative placental adherence, bladder injury, postpartum hemorrhage and caesarian hysterectomy respectively.

Conclusion: An unexplained elevated MSAFP level >2MOM, which is an objective method can be a more useful method in predicting intra-operative morbid placental adherence and intra-operative complications in cases of suspected morbidly adherent placenta.

Key Words: MSAFP – Ultrasound – Morbidly – Adherent placenta.

Introduction

PLACENTA accreta (morbidly adherent placenta), a condition in which all or part of the placenta adheres to the uterine wall owing to myometrial invasion by chorionic villi, occurs in 5% of women with placenta previa [1]. It may occur in settings of either primary deficiency or secondary damage to chronic villi or Nitabuch’s layer [2]. Factors associated with a higher incidence of placenta accreta include multiparity, prior uterine Surgery (myomectomy), advanced maternal age, placenta previa, prior uterine curettage, and previous caesarean section (CS) [2]. Uterine irradiation as an intra-abdominal Cancer Therapy has also been identified as a risk factor for percreta, a condition in which the illous invasion extends to or through the serosal covering of the uterus [3]. Placenta percreta has also been reported to occur after endometrial ablation [4] and represents one of the highest risk complications of pregnancy, with a 7% mortality rate even when 50% of patients treated for this condition are diagnosed preoperatively.

The antepartum diagnosis of placenta accreta/percreta is usually accomplished through ultrasound [5] or magnetic resonance imaging (MRI) [6]. Twickler et al., [7] reported that the two ultrasound criteria specific for accreta were myometrial thickness less than 1mm and large intraplacental blood lakes defined as placental lacunae by colour Doppler ultrasound enhancement. MRI should be considered in cases in which sonographic evaluation is inconclusive and there is a concern about invasion of trophoblasts into surrounding organs and tissues, especially if parametrial or posterior invasion is suspected [8,9]. The main MRI features of placenta accreta include uterine bulging, heterogeneous signal intensity within the placenta, and dark intraplacental bands on T2-weighted imaging [10].

Abnormally elevated alpha-fetoprotein (AFP) level in the second trimester has been associated
with placenta accrete, and it has been suggested that there is a direct relationship between the extent of invasion and the elevation of the [11] Unexplained elevation of maternal serum AFP (MSAFP) level has been typically defined as AFP level > 2 multiples of the median (MoM) in the absence of chromosomal abnormalities; foetal structural anomalies (e.g. open neural defects, abdominal wall defect); placental anomalies such as chorioangioma, multiple pregnancy, or foetal demise; or maternal conditions such as ovarian tumour or choriocarcinoma [12].

Placenta accreta should also be suspected in pregnant women with elevated MSAFP levels, with no other obvious cause. The defect in the layer normally separating the placenta and uterus allows leakage of foetal AFP into the mother's circulation. Up to 45% of women with placenta accreta have elevated MSAFP levels in the absence of an obvious cause [13]. Therefore, the aim of the current study was to examine the unexplained increase in MSAFP levels and ultrasound criteria in predicting the extent of invasion as well as intra-operative morbidity in cases of suspected morbid adherence of the placenta.

Material and Methods

A prospective cohort study was conducted in Ain Shams University Maternity Hospital from March 2012 – December 2012. The study was approved by The Local Ethical and Research Committee of Ain Shams University Maternity Hospital. All research were conducted in accordance with the ethical principles for medical research involving human subjects of the world medical association (WMA: Declaration of Helsinki), as revised during the 95th WMA general assembly held in Seoul, South Korea in October 2008.

The current study included female participants 19-42 years of age who were pregnant with a single foetus. All participants had a prior uterine scar and were at 24 weeks of gestation or more. Additionally, all had undergone abdominal ultrasounds showing placenta previa anterior or overlying the scar, with criteria suggestive of invasion by ultrasound: myometrial thickness less than 1mm; large intraplacental blood lakes, defined as placental lacunae by colour Doppler ultrasound enhancement; loss of the retroplacental sonolucent zone; thinning or disruption of the hyperechoic serosa-bladder interface; and presence of focal exophytic masses invading the urinary bladder. Each criterion was given a score of (1) present or (0) absent, and each patient was given a total sonographic score from 0 to 5. Women pregnant before 24 weeks of gestation and those with multiple gestations were excluded from the study. Additionally, pregnant women with other causes of elevated MSAFP (e.g. congenital fatal malformations, ovarian tumours with pregnancy) were also excluded.

After confirming the inclusion criteria, written informed consent was obtained from participants. A venous blood sample was collected, centrifuged, and analysed immediately using an enzyme-linked immunosorbent assay (ELISA). The MSAFP cutoff value of 2MoM was used to provide the best combination of sensitivity and specificity for the outcome [12].

Statistical analysis:

Regarding the sample size, data from a previous relevant study showed that the sensitivity of elevated MSAFP level in the prediction of morbidly adherent placenta in women with placenta previa was 45.5% [11]. Calculation of values to produce the least statistically acceptable figures resulted in a minimal sample size of 60 cases.

Results

A total of 60 pregnant women with at least one previous caesarean section (CS) and placenta previa or placenta anterior overlying the scar were included. The median number of previous CS in the study population was 3 (Fig. 1). The distribution of the ultrasound score for placental morbid adherence among the studied cases is shown in (Fig. 2), and the distribution of different morbidities encountered intra-operatively is shown in Table (1).

The median MSAFP concentration in the included women was 225ng/mL (range: 42-1000; interquartile range: 104.2-380ng/mL). Fourteen (23.3%) participants had MSAFP levels <2MoM, 44 (73.3%) had levels ranging from 2 to 2.5MoM, and only two (3.3%) had levels >2.5MoM.

A sonographic score >3 was associated with morbid placental adherence at a sensitivity of 82.6%, a specificity of 92.1%, a positive predictive value (PPV) of 97.4%, a negative predictive value (NPV) of 61.9%, a positive likelihood ratio (LR+) of 11.6, and a negative likelihood ratio (LR) of 0.2. The association between different sonographic findings and intra-operative morbidities is shown in Table (2). Study results also indicated a significant positive correlation between MSAFP and sonographic score for morbid placental adherence according to the Spearman’s rank correlation coefficient ($r^2=0.574$, $p<0.001$).
MSAFP >2MoM was significantly associated with an almost 3-fold, 7-fold, 2-fold, and 3-fold higher risk of intra-operative morbid placental adherence, bladder injury, postpartum haemorrhage (PPH), and caesarean hysterectomy, respectively. A serum AFP >2MoM was associated with morbid placental adherence at a sensitivity of 93.3%, a specificity of 71.4%, a PPV of 91.3%, a NPV of 71.4%, a LR+ of 3.2, and a LR of 0.1.

The receiver operator characteristic curve constructed for MSAFP as a predictor of morbid placental adherence showed significant predictability (area under the curve: 0.828; 95% confidence interval: 0.703-0.954, \( p < 0.001 \)) with serum AFP level >2MoM associated with morbid placental adherence and intraoperative complications (Fig. 3).

Table (1): Intra-operative events in women included in this study.

<table>
<thead>
<tr>
<th>Morbid Adherence</th>
<th>PPH</th>
<th>Blood transfusion</th>
<th>Caesarean hysterectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>46 (76.7%)</td>
<td>45 (75%)</td>
<td>47 (78.3%)</td>
<td>43 (71.7%)</td>
</tr>
<tr>
<td>45 (75%)</td>
<td>47 (78.3%)</td>
<td>43 (71.7%)</td>
<td>47 (78.3%)</td>
</tr>
<tr>
<td>5-8 units</td>
<td>15 (25%)</td>
<td>24 (40%)</td>
<td>20 (33.3%)</td>
</tr>
<tr>
<td>&gt;8 units</td>
<td>5 (8.3%)</td>
<td>6 (10%)</td>
<td>6 (10%)</td>
</tr>
</tbody>
</table>

Table (2): Association between sonographic signs of adherence and intra-operative complications in women included in this study.

<table>
<thead>
<tr>
<th>Intra-operative morbid adherence</th>
<th>Bladder injury</th>
<th>PPH</th>
<th>Blood transfusion &gt;4 units</th>
<th>Caesarean hysterectomy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of retroplacental zone</td>
<td>1.02 (0.57-1.83)</td>
<td>1.64 (0.29-9.26)</td>
<td>1.0 (0.17-5.79)</td>
<td>0.82 (0.42-1.32)</td>
</tr>
<tr>
<td>Myometrial thickness &lt;1mm</td>
<td>4.4 (1.27-15.2)</td>
<td>3.2 (0.85-17.6)</td>
<td>2.8 (1.08-7.25)</td>
<td>3.8 (0.57-25.01)</td>
</tr>
<tr>
<td>Abnormal placental lacunae</td>
<td>1.89 (1.26-2.84)</td>
<td>1.62 (0.79-3.3)</td>
<td>1.64 (1.12-2.42)</td>
<td>2.0 (0.84-4.78)</td>
</tr>
<tr>
<td>Thinning or disruption of serosa-bladder interface</td>
<td>1.62 (1.21-2.18)</td>
<td>4.35 (1.87-10.1)</td>
<td>1.72 (1.25-2.35)</td>
<td>3.42 (1.43-8.26)</td>
</tr>
<tr>
<td>Focal exophytic masses invading the bladder</td>
<td>1 (1.23-1.93)</td>
<td>3.33 (1.78-6.25)</td>
<td>1.6 (1.26-2.03)</td>
<td>372 (1.76-7.81)</td>
</tr>
</tbody>
</table>

Data presented as relative risks and their 95% confidence intervals. PPH: Postpartum haemorrhage.

Fig. (1): Pie-chart showing the distribution of the number of previous CS in the women included in this study.

Fig. (2): Pie-chart showing sonographic scores for placental morbid adherence in women included in this study.
Discussion

To the best of our knowledge, no studies reported in the literature have examined the relationship between elevated levels of MSAFP and sonographic scores of morbid placental adherence regarding prognosis in pregnancies with suspected morbidly adherent placenta and without a MSAFP cutoff. The results of our study showed that, compared to a sonographic score >3, MSAFP >2MoM showed a more significant positive correlation with intra-operative complications of morbid placental adherence, bladder injury, PPH, and caesarean hysterectomy.

The results of the current study are in good agreement with the results of several studies, but differed from the results generated by others. Shih et al., [5] showed that among 72 women with placenta previa and a previous CS, a sonographic score >3 was associated with morbid placental adherence in 38 of the women with a previous CS and placenta previa (sensitivity, 95%; specificity, 76%; PPV, 82%) and with an almost 2-fold, 4-fold, and 3-fold risk of intra-operative complications of morbid placental adherence, bladder injury, PPH, and caesarean hysterectomy, respectively.

The association that was detected between sonographic signs for morbid placental adherence and intra-operative complications shown in Table (2) is in good agreement with the observations of Twickler et al., [7,18,19], who reported that myometrial thickness <1mm and large intraplacental blood lakes defined as placental lacunae by colour Doppler ultrasound enhancement were two ultrasound criteria specific of accreta.

The results of our study are also in agreement with those of Zelop et al., [11] who reviewed the MSAFP levels of 11 women who had caesarean hysterectomies because of placenta accreta. The control group consisted of 14 women who had delivered by CS because of placenta previa without morbidly adherent placenta. Five of the 11 women with placenta accreta had elevated MSAFP levels, whereas all 14 controls had normal levels. These results indicated a significant association between elevated MSAFP levels and morbidly adherent placenta. Patients with an unexplained elevation of MSAFP levels in addition to placenta previa may be at increased risk for morbidly adherent placenta.

Additionally, an increased frequency of persistent placenta previa and abnormal placental invasion has also been described in case reports and in case-control and cohort studies in association with MSAFP >2MoM [14-16].

However, our results contrasted with those of Erin et al., [17] which showed that women with a MSAFP level of at least 2.0MoM and placenta previa were significantly more likely to be hospitalised for bleeding before 30 weeks of gestation, to be delivered preterm, and to be delivered for pregnancy-associated hypertension before 34 weeks of gestation. However, there were no significant differences between groups regarding placental separation, placenta accreta, and non-elective caesarean hysterectomy. Women with placenta previa and MSAFP elevation had a risk of placenta accreta of more than 50% (21% vs 13%, p=0.39), but that difference did not reach the level of statistical significance, possibly due to the small sample size.

Conclusion:

MSAFP can predict intra-operative complications of morbid placental adherence, caesarean hysterectomy, bladder injury, and PPH, with a predictive value similar to that of sonographically detected myometrial thickness <1mm and the presence of abnormal placental lacunae. However, none of these methods used alone are sufficient in a Clinical setting. Therefore, the cutoff of MSAFP >2MoM and a sonographic score >3 together may be more useful in predicting intra-operative morbid placental adherence, which strongly necessitates special precautions before Surgical intervention.

References


