Predictive effect of umbilical artery color Doppler ultrasonography on adverse pregnancy outcomes in systemic lupus erythematosus patients combined with gestational hypertension

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Received July 24, 2019; Accepted October 9, 2019; Epub December 15, 2019; Published December 30, 2019

Abstract: Objective: To explore the predictive effect of umbilical artery color Doppler ultrasonography on adverse pregnancy outcomes in systemic lupus erythematosus (SLE) patients combined with gestational hypertension. Methods: A total of 124 SLE pregnant patients were retrospectively analyzed, of which SLE patients combined with gestational hypertension suffering from adverse pregnancy outcomes (case group), and those not suffering from adverse pregnancy outcomes (control group) were compared in terms of parameters measured by umbilical artery color Doppler ultrasonography, including pulsatility index (PI), resistance index (RI), and ratio of systolic peak blood flow rate to end diastolic blood flow rate (S/D), and a receiver operating characteristic (ROC) curve was drawn to analyze the predictive effect of those parameters on adverse pregnancy outcomes in SLE patients combined with gestational hypertension. Results: The case group showed significantly higher PI, RI and S/D than the control group (all P<0.05). The area under ROC curve and 95% confidence interval (CI) of PI were 0.840 (P=0.001) and 0.674-1.000, respectively; those of RI were 0.770 (P=0.007), and 0.615-0.925, respectively, and those of S/D were 0.760 (P=0.009) and 0.570-0.949, respectively. Conclusion: Umbilical artery hemodynamic indexes including PI, RI and S/D have good predictive value for adverse pregnancy outcomes and they are worthy of clinical promotion and application.

Keywords: Umbilical artery color Doppler ultrasonography, systemic lupus erythematosus, gestational hypertension, pregnancy outcome

Introduction

Systemic lupus erythematosus (SLE), which commonly occurs in young women, is an autoimmune disease that usually involves multiple organs of the whole body; regardless most female patients choose pregnancy and delivery when the frequency of SLE is reduced and the condition is stable [1, 2]. However, clinical findings have revealed that pregnancy induces SLE to some extent, therefore SLE patients often suffer adverse pregnancy reactions during pregnancy, of which gestational hypertension occurs with relatively high incidence in SLE patients during pregnancy [3, 4]. Gestational hypertension, as an obstetric complication, poses a great threat to life safety. Fetuses absorb nutrition through umbilical arteries during pregnancy, but the vascular resistance in the uterus and placenta in gestational hypertension patients is increased significantly, and the blood flow through them is correspondingly slowed down, which results in frequent fetal hypoxia and ischemia [5, 6].

Pregnancy with SLE and gestational hypertension induces a high risk pregnancy. Clinical statistics reveal that SLE patients combined with gestational hypertension are prone to adverse pregnancy outcomes during pregnancy, such as premature delivery and intrauterine asphyxia, which brings heavy psychological and economic burden to patients [7, 8]. SLE patients combined with gestational hypertension show
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changes in fetal umbilical artery hemodynamic parameters, including vascular resistance increase, and blood flow decrease; from which fetal growth and adverse pregnancy outcomes can be preliminarily inferred clinically according to umbilical artery blood flow. In umbilical artery color Doppler ultrasonography, resistance index (RI) reflects the peripheral resistance of umbilical artery, pulsatility index (PI) reflects the vascular elasticity, and the ratio of systolic peak blood flow rate to end diastolic blood flow rate (S/D) reflects the blood flow rate in umbilical arteries in a cardiac cycle. Generally, a longer gestational period is accompanied by constantly decreased PI, RI and S/D, and it has been confirmed clinically that umbilical arterial blood flow parameters are related to gestational hypertension and fetal growth and development [9-11]. In order to reduce the probability of adverse pregnancy outcomes in SLE patients combined with gestational hypertension, it is necessary to predict in a timely manner whether adverse pregnancy outcomes will occur or not, so as to terminate pregnancy before or at the initial pregnancy stage to avoid more serious pregnancy outcomes.

Umbilical artery color Doppler ultrasonography provides a prediction for the disease, but there is no comprehensive and in-depth clinical study about it, so there is not enough clinical data to support the predictive value of umbilical artery color Doppler ultrasonography for adverse pregnancy outcomes in SLE patients combined with gestational hypertension. Therefore, this study analyzed umbilical arterial blood flow parameters of SLE patients combined with gestational hypertension and SLE patients not combined with gestational hypertension, in order to explore the predictive value of the parameters for adverse pregnancy outcomes.

Materials and methods

Clinical data

The clinical data of 124 SLE patients combined with gestational hypertension admitted to Shandong Provincial Hospital Affiliated to Shandong University from March 2015 to February 2018 were collected, and the patients were divided into a case group and a control group according to whether adverse pregnancy outcomes occurred or not; of which the case group consisted of 35 patients who had adverse pregnancy outcomes with an average age of (30.4±4.3) years and pregnancy of (29.4±4.3) weeks, and the control group consisted of 89 patients who did not have adverse pregnancy outcomes with an average age of (31.3±4.5) years and pregnancy of (29.9±4.1) weeks. The study was approved by the Ethics Committee of Shandong Provincial Hospital Affiliated to Shandong University.

Inclusion criteria: Patients between 18 and 40 years old who met the diagnostic criteria of SLE combined with gestational hypertension [12].

Exclusion criteria: Patients with severe dysfunction of important organs such as heart, liver and kidney; patients combined with eclampsia; patients with essential hypertension or history of gynecologic malignant tumors; patients with a history of diabetes or combined gestational diabetes mellitus, history of habitual abortion, other combined rheumatic diseases other than SLE; patients with multiple pregnancy; patients without complete clinical data.

Color Doppler ultrasonography for umbilical arterial blood flow

A Philips EPIQ color Doppler ultrasound diagnostic instrument with a two-dimensional convex array probe at 2-5 MHZ in frequency was used to detect the umbilical cord cross section. The PI, RI and S/D were recorded using a blood flow spectrum. Among color Doppler ultrasound parameters, \( v_{\text{max}} \) was the maximum umbilical artery end systolic blood flow rate (S); \( v_{\text{min}} \) was the end diastolic blood flow rate (D); S/D was the ratio of S to D. PI=(S-D)/M, where M was the average value of the sums of \( v_{\text{max}} \) and \( v_{\text{min}} \). RI=(S-D)/S [13]. The above indexes were measured at the 29th week of pregnancy. Those indexes were recorded 3 times in succession in each examination, and the average blood flow rate was taken.

Observation indexes

(1) Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score: the two groups were scored based on SLEDAI before measurement according to their clinical symptoms [14]. (2) Adverse pregnancy outcomes: adverse pregnancy outcomes included abnormal birth body mass of newborns (less than two standard deviations of average body mass of newborns under the same gestational age and
Predictive effect of umbilical artery color Doppler ultrasonography

### Table 1. Comparison in general clinical data

<table>
<thead>
<tr>
<th>Group</th>
<th>Control group</th>
<th>Case group</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31.3±4.5</td>
<td>30.4±4.3</td>
<td>0.839</td>
</tr>
<tr>
<td>Pregnancy (weeks)</td>
<td>29.9±4.1</td>
<td>29.4±4.3</td>
<td>1.321</td>
</tr>
<tr>
<td>Primipara (n)</td>
<td>56</td>
<td>22</td>
<td>1.012</td>
</tr>
<tr>
<td>Systolic pressure (mmHg)</td>
<td>158.67±58.67</td>
<td>160.75±60.75</td>
<td>1.213</td>
</tr>
<tr>
<td>Obesity (n)</td>
<td>54</td>
<td>26</td>
<td>0.648</td>
</tr>
<tr>
<td>SLEDAI score</td>
<td>3.09±1.21*</td>
<td>6.32±1.51</td>
<td>0.021</td>
</tr>
</tbody>
</table>

Note: SLEDAI, Systemic Lupus Erythematosus Disease Activity Index. Note: *P<0.05 compared with the control group.

### Table 2. Incidence of adverse pregnancy outcomes in the case group

<table>
<thead>
<tr>
<th>Adverse pregnancy outcome</th>
<th>Case (n)</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal birth weight</td>
<td>18</td>
<td>51.43</td>
</tr>
<tr>
<td>Intrauterine distress</td>
<td>10</td>
<td>28.57</td>
</tr>
<tr>
<td>Premature delivery</td>
<td>2</td>
<td>5.71</td>
</tr>
<tr>
<td>Neonatal asphyxia</td>
<td>5</td>
<td>14.29</td>
</tr>
</tbody>
</table>

### Table 3. Comparison in parameters measured by umbilical artery color Doppler ultrasonography (x±sd)

<table>
<thead>
<tr>
<th>Group</th>
<th>PI</th>
<th>RI</th>
<th>S/D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case group (N=35)</td>
<td>1.05±0.21</td>
<td>0.74±0.11</td>
<td>3.21±0.21</td>
</tr>
<tr>
<td>Control group (N=89)</td>
<td>0.80±0.11</td>
<td>0.62±0.21</td>
<td>2.43±0.31</td>
</tr>
<tr>
<td>t</td>
<td>10.488</td>
<td>5.034</td>
<td>20.294</td>
</tr>
<tr>
<td>P</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: PI, pulsatility index; RI, resistance index; S/D, ratio of systolic peak blood flow rate to end diastolic blood flow rate.

same gender), intrauterine distress (the predictive criteria was heart rate deceleration for 2 consecutive beats or turbid amniotic fluid based on fetal heart rate monitoring), premature delivery (delivery of a live baby before 37 weeks of pregnancy), neonatal asphyxia (hypoxemia or hypercapnia due to inability of normal breathing autonomously in the intrauterine fetus within 1 minute of birth for lack of oxygen) [15].

**Statistical analysis**

Data were processed and analyzed using the statistical software SPSS 17.0. Measurement data were expressed as (x±sd), and differences between groups were checked by t-test. Enumeration data were expressed as n, and differences between groups were checked by chi-square test. P<0.05 indicated a significant difference. A receiver operating characteristic (ROC) curve was drawn and the area under the curve (AUC) of parameters in predicting adverse pregnancy outcomes was calculated.

**Results**

### Comparison in general clinical data

The two groups showed no significant difference in age, pregnancy, blood pressure, primipara identity and obesity (all P>0.05). The case group showed significantly higher SLEDAI score than the control group (P<0.05). More details are shown in Table 1.

**Incidence of adverse pregnancy outcomes in the case group**

The case group showed 18 newborns with abnormal birth weight (51.42%), 10 fetuses under intrauterine distress (28.57%), 2 patients with premature delivery (5.71%), and 5 newborns with neonatal asphyxia (14.28%). More details are shown in Table 2.

### Comparison in parameters measured by umbilical artery color Doppler ultrasonography

The pulsatility index, resistance index and S/D score of the case group were 1.05±0.21, 0.74±0.11 and 3.21±0.21, respectively, which is significantly higher than those of the control group (all P<0.001). More details are shown in Table 3. Typical umbilical artery color Doppler ultrasonography results of the case group and control group are shown in Figures 1 and 2.

**Prediction of adverse pregnancy outcomes in SLE patients combined with gestational hypertension based on parameters measured by umbilical artery color Doppler ultrasonography**

A ROC curve was drawn, the AUC, standard error, and 95% confidence interval of PI were 0.840, 0.085, and 0.674-1.000, respectively; those of RI were 0.770, 0.079, and 0.615-0.925, respectively, and those of S/D were 0.760, 0.097, and 0.570-0.949, respectively. More details are shown in Table 4 and Figure 3.
Discussion

SLE is an autoimmune disease common in childbearing age females, which is likely to cause premature delivery and intrauterine distress after onset [16, 17]. Pregnant women have increased probability of gestational hypertension during the 20th week of pregnancy. Gestational hypertension patients have significant placental blood flow decrease, systemic small vessel spasms, cardiac output decrease, peripheral resistance increase, myocardial perfusion decrease in many organs, and even hypoxia-ischemia of tissues, which leads to hypertension, proteinuria, edema, and other clinical manifestations in gestational hypertension patients. This disease usually causes premature delivery, intrauterine asphyxia and other severe complications due to ineffective treatment and fast onset, which brings safety problems to both patients and fetuses. In addition, it has an annual increasing incidence. Therefore, this disease has been regarded as an important clinical research topic [18].

Pregnancy with SLE and gestational hypertension causes high risk pregnancy. Patients with such pregnancy are more prone to adverse pregnancy outcomes than healthy pregnant women. Their adverse pregnancy outcomes are usually serious, and their treatment is usually undesired. Clinically, it is believed that active measures should be taken early to predict the probability of adverse pregnancy outcomes in SLE patients combined with gestational hypertension, so as to reduce serious maternal and infant health and safety problems.

SLE patients combined with gestational hypertension are accompanied with continuous

Figure 1. Umbilical artery color Doppler ultrasonography in systemic lupus erythematosus combined with gestational hypertension patient (patient with adverse pregnancy outcome). A 31-year-old woman at 30 weeks of gestation had a PI of 1.21, a RI of 0.69 and a S/D of 3.2. PI, pulsatility index; RI, resistance index; S/D, ratio of systolic peak blood flow rate to end diastolic blood flow rate.

Figure 2. Umbilical artery color Doppler ultrasonography in systemic lupus erythematosus combined with gestational hypertension patient (patient without adverse pregnancy outcome). A 29-year-old woman at 29 weeks of gestation had a PI of 0.89, a RI of 0.58 and a S/D of 2.4. PI, pulsatility index; RI, resistance index; S/D, ratio of systolic peak blood flow rate to end diastolic blood flow rate.
increase of umbilical artery vascular permeability, so plasma exudation will lead to hemoconcentration, increased blood flow resistance, and increased blood pressure, thus leading to a variety of adverse pregnancy outcomes, such as premature delivery, intrauterine distress, and even maternal and fetal death. Mothers and fetuses exchange nutrition and gas mainly through the umbilical cord, so abnormality and placenta perfusion in umbilical arteries are shown as changes in umbilical arterial blood flow parameters [19]. Clinically, it is found that SLE patients combined with gestational hypertension are accompanied with vasospasms, smaller vascular caliber, and resistance increases, so the nutrition supplied to fetuses are reduced, and metabolites and toxins from them cannot be discharged in time, causing the fetus to be prone to adverse events. Therefore, detecting umbilical arterial blood flow parameters through umbilical artery color Doppler ultrasonography is of great significance for understanding the growth of fetuses. Umbilical arterial blood flow parameters can reflect umbilical artery vascular resistance. Under normal clinical conditions, pregnant women are accompanied with placental peripheral resistance decreases, blood flow increases, and significant increases of the main umbilical arterial blood flow parameters such as PI, RI and S/D; however, SLE patients combined with gestational hypertension show continuous increases of umbilical arterial blood flow parameters due to resistance increases, which are significantly different from healthy pregnant women, therefore fetal development can be estimated based on umbilical arterial blood flow parameters. In terms of umbilical artery parameters, S/D reflects the placental vascular resistance. Clinically, it is shown that if S/D value increases significantly in late pregnancy, the possibility of adverse pregnancy outcomes increases. RI is the ratio of blood flow rate change to maximum systolic blood flow rate in a cardiac cycle. RI increase mostly indicates fetal intrauterine hypoxia. PI is the ratio of diastolic blood flow rate change to average blood flow rate in a cardiac cycle, and PI change may indicate fetal intrauterine ischemia [19, 20]. Analyzing the above parameters jointly is of great significance to the prediction of adverse pregnancy outcomes, which indicates that umbilical artery color Doppler ultrasonography may be an important means to detect adverse pregnancy outcomes in SLE patients combined with gestational hypertension.

In this study, the case group showed significantly higher umbilical artery blood flow parameters including PI, RI and S/D than the control group (all P<0.05), which indicated that blood flow parameters have relatively high predictive value in adverse pregnancy outcomes. Clinically, it is suggested that more close monitoring and more attention can be paid when the parameter levels exceed the optimal predictive thresholds, and other monitoring methods can also be adopted together to find adverse pregnancy outcomes and prevent adverse pregnancy from becoming more serious, if necessary. A experiment by Wang found that the specificity of parameters measured by umbilical artery color Doppler ultrasonography, PI, RI and S/D to adverse pregnancy outcomes were 88.4%, 83.7% and 88.4%, respectively, which further supported the our study results [21]. A ROC curve was drawn, and it was found that the AUC of PI, RI and S/D was 0.840 (P=0.001), 0.770 (P=0.007), and 0.760 (P=0.009), respectively. AUC of the three indexes was within the range of 0.7-0.9, which indicated that the three indexes had strong diagnostic value for adverse pregnancy outcomes. The disadvantages of this study were as follows: only PI, RI and S/D were adopted to predict adverse pregnancy outcomes, so subsequent studies could select multiple umbilical arterial blood flow parameters for analysis and study, so as to provide more clinical data. In addition, this study only studied the overall prediction of blood flow parameters on adverse pregnancy outcomes. In the future, studies can focus on the monitor-

<table>
<thead>
<tr>
<th>Index</th>
<th>AUC</th>
<th>Standard error</th>
<th>95% confidence interval</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>PI</td>
<td>0.840</td>
<td>0.085</td>
<td>0.674-1.000</td>
<td>0.001</td>
</tr>
<tr>
<td>RI</td>
<td>0.770</td>
<td>0.079</td>
<td>0.615-0.925</td>
<td>0.007</td>
</tr>
<tr>
<td>S/D</td>
<td>0.760</td>
<td>0.097</td>
<td>0.570-0.949</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Note: PI, pulsatility index; RI, resistance index; S/D, ratio of systolic peak blood flow rate to end diastolic blood flow rate; AUC, area under the receiver operating characteristic curve.
Predictive effect of umbilical artery color Doppler ultrasonography

Predicting value of blood flow parameters on a single adverse pregnancy outcome.

To sum up, if adverse pregnancy outcomes of SLE patients combined with gestational hypertension can be predicted by umbilical artery examination, analyzing the PI, RI and S/D in the examination can increase the prediction accuracy, and corresponding preventive measures can be taken to reduce the possibility of adverse pregnancy outcomes.

Acknowledgements

This work was supported by Medical and Health Science and Technology Development Program of Shandong Province (2014WS0073) and Key R&D Projects of Shandong Province (Public Welfare Projects) (2018GSF118112).

Disclosure of conflict of interest

None.

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References


Figure 3. Predicting ROC of adverse pregnancy outcomes in SLE patients combined with gestational hypertension detected by umbilical artery color Doppler ultrasonography. PI, pulsatility index; RI, resistance index; S/D, ratio of systolic peak blood flow rate to end diastolic blood flow rate; ROC, receiver operating characteristic.


