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The relationship between clinical characteristics and pregnancy outcome in preeclamptic patients

Yoshiko Shiroshita¹, Masanobu Ohashi², and Hiroya Matsuo¹

The aim of this study is to investigate the association between the maternal characteristics of preeclamptic women and the severity of preeclampsia, mode of delivery and incidence of intrauterine growth retardation (IUGR). We examined retrospectively the medical records of 58 patients with preeclampsia who gave birth at Hyogo Children’s Hospital from January to December 2001. The older is the maternal age, the higher is the incidence of early onset preeclampsia. The incidence of severe preeclampsia in primiparae aged ≥35 years is higher than that in multiparae aged ≥35 years. Severe preeclamptic patients showed a higher positive rate of family history of hypertension (37.2%) compared with that in mild preeclamptic patients (26.7%). The frequency of >8 kg weight gain among patients with severe preeclampsia was lower compared with that among patients with mild preeclampsia. The birth weight of infants in primiparae with early onset preeclampsia was significantly lighter than that in other preeclamptic patients (P<0.05). Moreover, there was a significant relationship between mode of delivery and the birth weight or the placental weight in primiparae complicated with late onset preeclampsia (≥35 week termination) (P<0.05). It could be probable that maternal characteristics of preeclamptic patients were important for the prediction of the severity of preeclampsia, IUGR and mode of delivery.

Key Words
Preeclampsia, maternal characteristics, pregnancy outcome.

Introduction

Preeclampsia is a pregnancy-specific syndrome of reduced organ perfusion secondary to vasospasm and endothelial activation. This is thought to have an impact on 6% to 10% of pregnancies and is a relatively common complication of pregnancy and forms a major cause of maternal, fetal, and neonatal morbidity and mortality¹-⁴. Although the management and prevention of preeclampsia have improved so much in the present time, the syndrome of preeclampsia is still one of the major pregnancy disorders⁵,⁶.

Preeclampsia is twice as common in primiparae as in multiparae⁷. Previous studies have identified primiparae as one of the risk factors, together with advanced maternal age, diabetes mellitus, obesity, multiple gestations, urinary tract infection, and autoimmune disease⁸-¹¹. Apart from these, risk factors include genetic, ethnic factors¹²,¹³, and life style related factors. Until now, numerous risk factors for preeclampsia have been suggested. However, little information is available on how maternal characteristics
as risk factors relate to the severity or mode of delivery in preeclamptic patients. On the other hand, the success of preventive intervention depends on the possibility of recognizing the early, latent stage of the disease by means of reliable and acceptable predictive tests and on the availability of effective methods of intervention. But this was hampered by the fact that as yet no reliable and acceptable screening tests for women at risk are available.

It is clinically very important for the evaluation of pregnancy outcome of preeclamptic patients to comprehend the maternal characteristics before delivery. Thus, in the present study, we investigated the association between the maternal characteristics of preeclamptic women and the severity of preeclampsia, mode of delivery and incidence of IUGR.

Subjects and Methods

1. Subjects

This study consisted of a retrospective review of the medical records of the patients who were admitted with a diagnosis of preeclampsia from January to December 2001, at Hyogo Children’s Hospital. The following data were evaluated: maternal age, parity, family history of hypertension (both maternal and paternal hypertension), pre-pregnancy BMI, weight gain, onset and severity of preeclampsia, incidence of IUGR, mode of delivery, birth weight and placental weight. Maternal age was categorized into six groups: less than 20 years, 20–24 years, 25–29 years, 30–34 years, 35–39 years, and more than 40 years. BMI was calculated as weight (kg)/height (m²). Early onset of preeclampsia was defined as onset of disease at less than 32 weeks of gestation.

This retrospective study received approval from the Institutional Review Board at Kobe University School of Medicine. Informed consent for the use of the medical records for the present study was obtained from Hyogo Children’s Hospital before the study.

2. Patients background

The study population included 58 preeclamptic patients, consisting of 37 primiparae and 21 multiparae. There were 15 patients with mild preeclampsia and 43 patients with severe preeclampsia. Then, there were 30 patients complicated by early onset of the disease while 28 patients had late onset of disease.

The mean age of the 37 primiparae was 30.4±6.3 (mean±SD), which was higher than that of Japanese primiparae who gave birth in the year 2001 in Japan\(^{10}\). The mean age of 21 multiparae

A)

<table>
<thead>
<tr>
<th></th>
<th>mean±SD</th>
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<tbody>
<tr>
<td>p.p.</td>
<td>30.4±6.3</td>
</tr>
<tr>
<td>m.p.</td>
<td>32.6±4.3</td>
</tr>
</tbody>
</table>

B)

![Fig. 1 Maternal age of patients. The mean age of 37 primiparae was 30.4±6.3 (mean±SD) and the mean age of 21 multiparae was 32.6±4.3 (mean±SD). p.p.: primiparae, m.p.: multiparae(A). Of the 58 patients, there were 17 patients aged ≥35 years, and they accounted for 29.3% of total data (B).](image-url)
Pregnancy outcome of preeclampsia

Table 1. Characteristics of patients (N=58)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Age (yr)</th>
<th>Parity</th>
<th>Family history</th>
<th>Pre-pregnancy BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>31.4±5.7</td>
<td>p.p.</td>
<td>hypertension</td>
<td>21.1±5.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>37 (63.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>m.p.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>21 (36.2%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p.p.: primipara, m.p.: multipara.

was 32.6±4.3 (mean±SD) (Fig.1 A). Patients aged ≥35 years accounted for 29.3% (n=17) of total data (Fig.1 B). Table 1 summarizes the characteristics of patients.

58 patients were divided into four groups (primiparae with early onset preeclampsia (N=14), primiparae with late onset preeclampsia (N=23), multiparae with early onset preeclampsia (N=16), multiparae with late onset of preeclampsia (N=5)). The incidence of severe preeclampsia was evaluated in every group.

3. Pregnancy outcome evaluation

Data of patients who delivered at a gestational age of ≥35 weeks were extracted to evaluate the relationship between maternal weight gain and the severity of preeclampsia. Of the 58 patients who developed preeclampsia, there were 35 patients with ≥35–week termination. Of these, the data on maternal weight gain from 33 patients was available for this analysis.

Next, we investigated the impact of parity and onset of disease on the severity of preeclampsia or fetal growth. Of the 35 patients with ≥35–week termination, 5 patients were excluded because of multiple gestation, one of the predisposing factors of preeclampsia. Therefore, data of 30 patients were available and these patients were divided into four groups for analysis (primiparae with early onset preeclampsia (N=3), primiparae with late onset preeclampsia (N=19), multiparae with early onset preeclampsia (N=3), multiparae with late onset of preeclampsia (N=5)). The following factors were evaluated in each group: maternal age, termination, the proportion of severe preeclampsia and IUGR, mode of delivery (cesarean section or vaginal delivery), birth weight and placental weight. Finally, the 19 primiparae complicated with late onset preeclampsia (≥35–week termination) were evaluated further in order to determine the factors impacted on mode of delivery and divided these 19 patients into two groups according to mode of delivery: 8 patients who underwent cesarean section and 11 patients who underwent vaginal delivery.

4. Statistical analyses

Statistical analyses were performed with Statcel with the Chi-square test, the Fisher exact test and the t-test. Statistical significance was considered to be present at P<0.05.

Results

1. Maternal age, parity, onset and severity of preeclampsia

Increased rates of early onset preeclampsia were associated with advancing maternal age (Fig.2). Of the 17 patients aged ≥35 years, 10 were primiparae and 7 were multiparae. Of the 10
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Figure 2 The maternal age and early onset of preeclampsia. There were increasing incidences of the early onset with advancing age.

Figure 3 Rates of preeclampsia of four groups classified by parity and onset. p.p.: primiparae, m.p.: multiparae.

Table 2. Parity and severity in preeclamptic patients aged ≥35 years

<table>
<thead>
<tr>
<th>Parity</th>
<th>Mild (N=4)</th>
<th>Severe (N=13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>p.p. (N=10)</td>
<td>1 (10%)</td>
<td>9 (90%)</td>
</tr>
<tr>
<td>m.p. (N=7)</td>
<td>3 (42.9%)</td>
<td>4 (57.1%)</td>
</tr>
</tbody>
</table>


Table 3. Family history of hypertension and severity of disease

<table>
<thead>
<tr>
<th>Family history (+)</th>
<th>Mild (N=15)</th>
<th>Severe (N=43)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>4 (26.7%)</td>
<td>16 (37.2%)</td>
</tr>
</tbody>
</table>

N(%), Mild: mild preeclampsia, Severe: severe preeclampsia.

2. Family history of hypertension and severity of preeclampsia

Of the 15 patients with mild preeclampsia, there were 4 (26.7%) patients who have a positive family profile for hypertension. On the other hand, of the 43 patients with severe preeclampsia, there were 16 (37.2%) patients with a family history of hypertension. The incidence of family history of hypertension in patients complicated with severe preeclampsia was slightly higher than that in patients complicated with mild preeclampsia, but the difference between these two groups was not statistically significant (the Fisher exact test) (Table 3).

3. Pre-pregnancy BMI, maternal weight gain and severity of preeclampsia

Of the 12 patients with mild preeclampsia, there were 9 (75.0%) patients who...
had >8 kg weight gain, as shown in Table 4. Of the 21 patients with severe preeclampsia, there were 11 (52.4%) patients with >8 kg weight gain. The frequency of >8 kg weight gain among patients with severe preeclampsia was slightly lower compared with that among patients with mild preeclampsia, but the difference between these two groups was not statistically significant (the Fisher exact test). On the other hand, there was no association between pre-pregnancy BMI and the severity of preeclampsia (data not shown).

4. Severity of preeclampsia and mode of delivery (≥35-week termination)

The group of primiparae with early onset preeclampsia showed the highest proportion of IUGR among the four groups. All patients of this group developed severe preeclampsia. The mode of delivery in the group of primiparae with early onset preeclampsia was the same as that of multiparae. However, birth weight in this group was significantly lower compared to those in other groups (P < 0.05), even though placental weight was within normal limits (490 g). The birth weight of one of primiparae with early onset preeclampsia was extremely low (848 g), followed by the significant difference.

5. Mode of delivery in primiparae complicated with late onset preeclampsia (≥35-week termination)

Table 6 showed the comparison of patients’ backgrounds, severity of preeclampsia and fetal growth between vaginal delivery and cesarean section in primiparae complicated with late onset preeclampsia (≥35-week termination). The patients who underwent cesarean section were rather older and had a higher incidence of family history compared with ones...

Table 4. Maternal weight gain and severity of preeclampsia (≥35-week termination)

<table>
<thead>
<tr>
<th></th>
<th>Mild (N=12)</th>
<th>Severe (N=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥8 kg weight gain</td>
<td>3 (25.0%)</td>
<td>10 (47.6%)</td>
</tr>
<tr>
<td>&lt;8 kg weight gain</td>
<td>9 (75.0%)</td>
<td>11 (52.4%)</td>
</tr>
</tbody>
</table>

N(%) ; Mild ; mild preeclampsia. Severe ; severe preeclampsia

Table 5. Severity of preeclampsia and fetal growth restriction (≥35-week termination)

<table>
<thead>
<tr>
<th></th>
<th>p.p. early (N=3)</th>
<th>p.p. late (N=19)</th>
<th>m.p. early (N=3)</th>
<th>m.p. late (N=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (yr)</td>
<td>28.0±2.0</td>
<td>29.2±6.0</td>
<td>36.0±6.1</td>
<td>32.4±3.9</td>
</tr>
<tr>
<td>Termination (wk)</td>
<td>36.9±0.5</td>
<td>38.0±1.4</td>
<td>37.1±1.7</td>
<td>38.7±0.7</td>
</tr>
<tr>
<td>Severe preeclampsia</td>
<td>3 (100.0%)</td>
<td>14 (73.7%)</td>
<td>2 (66.7%)</td>
<td>1 (20.0%)</td>
</tr>
<tr>
<td>IUGR</td>
<td>2 (66.7%)</td>
<td>9 (47.4%)</td>
<td>1 (33.3%)</td>
<td>2 (40.0%)</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>1599±871</td>
<td>2389±562</td>
<td>2297±545</td>
<td>2910±593</td>
</tr>
<tr>
<td>Placental weight (g)</td>
<td>490±111</td>
<td>446±131</td>
<td>450±63</td>
<td>540±214</td>
</tr>
</tbody>
</table>

mean±SD, N(%)  p.p. early : primiparae with early onset, p.p. late : primiparae with late onset. m.p. early : multiparae with early onset, m.p. late : multiparae with late onset. *P<0.05 VS p.p. late, m.p. early or m.p. late
Table 6. Mode of delivery in primiparae complicated with late onset preeclampsia (≥35-week termination)

<table>
<thead>
<tr>
<th></th>
<th>Vaginal delivery (N=8)</th>
<th>Cesarean section (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age (yr)</td>
<td>27.1±5.6</td>
<td>30.7±5.6</td>
</tr>
<tr>
<td>Family history (hypertension)</td>
<td>3 (37.5%)</td>
<td>5 (45.5%)</td>
</tr>
<tr>
<td>Pre-pregnancy BMI</td>
<td>22.6±4.3</td>
<td>22.5±3.8</td>
</tr>
<tr>
<td>Maternal weight gain</td>
<td>9.8±4.5</td>
<td>11.2±5.4</td>
</tr>
<tr>
<td>Severe preeclampsia</td>
<td>5 (62.5%)</td>
<td>10 (90.9%)</td>
</tr>
<tr>
<td>IUGR</td>
<td>3 (37.5%)</td>
<td>6 (54.6%)</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>2686±497</td>
<td>2174±525*</td>
</tr>
<tr>
<td>Placental weight (g)</td>
<td>515±131</td>
<td>397±112*</td>
</tr>
</tbody>
</table>

mean±SD, N (%)  *P<0.05

who had vaginal delivery. They also indicated higher proportions of severe preeclampsia and IUGR. There were significant differences between vaginal delivery group and cesarean section group in both birth weight and placental weight (P<0.05). However, there was no significant difference in pre-pregnancy BMI and maternal weight gain.

Discussion

Many researchers have demonstrated that advanced maternal age was associated with poor maternal and fetal outcomes. Tan K. T. and Tan K. H. reviewed the most common pregnancy complications in primigravid women older than age 35 years, compared with those in average-age (aged 25–34) and younger mothers (under 25)\(^{15}\). They found a 17% incidence of preeclampsia in this age group, compared with 10.8% in the control group. Barton J. R. et al. found that the frequency of preeclampsia in women older than age 35 was almost 3 times the rate of their younger counterparts\(^{16}\). Lee C. J. et al. also found that older women were at increased risk of preeclampsia\(^{19}\). Such an association may be related to the progressive vascular endothelial damage that occurs with aging.

In the present study, we showed that the incidence of severe preeclampsia (90%) in primiparae aged≥35 years was higher compared with that in multiparae aged≥35 years (57.1%). We demonstrated the relationship between advanced maternal age and early onset of preeclampsia which is predisposed to an increased risk of severe preeclampsia, and the increased risk of severe preeclampsia in primiparae aged≥35 years could be attributable to the high incidence of early onset of the disease. These results indicated that aged primiparae should be followed carefully for the possible development of preeclampsia.

Family studies have shown that genetic factors play a role in preeclampsia. Preeclampsia occurs at higher rates in sisters, daughters, and mothers of affected women\(^{17-20}\) and these epidemiological factors of preeclampsia suggest a genetic basis for the disease as demonstrated by Qiu C. et al.. Compared with women with no parental history of hypertension, women with maternal only, paternal only,
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or both maternal and paternal history of hypertension had statistically significant increased risk of preeclampsia (odds ratio = 1.9, 1.8, 2.6, respectively). The odds ratio for women with at least one hypertensive parent and a hypertensive sibling was 4.7.

In our study, we showed that the rate of positive family history of hypertension in severe preeclamptic patients was slightly higher (37.2%), compared with that in mild preeclamptic patients (26.7%). This finding indicated that family history might be an important genetic factor predisposed to not only the increased occurrence of preeclampsia but also the severity of preeclampsia.

It is well-known that women with obesity are at increased risk for complications that include hypertension, preeclampsia, gestational diabetes mellitus, cesarean section, and macrosomia. Ehrenberg H. M. et al. showed that the risk of perinatal complications, including preeclampsia and cesarean section, increased with maternal obesity. Inconsistent with previous reports, we found no relationship between pre-pregnancy BMI and the incidence of cesarean section. Nevertheless, our study indicated that the rate of patients who had >8 kg weight gain was slightly higher among the patients with mild preeclampsia compared with the patients with severe preeclampsia. Our findings were implied that maternal weight gain relates to mild preeclampsia rather than severe preeclampsia. It seems likely that the development of severe preeclampsia is associated neither with maternal obesity nor excessive weight gain but with genetic factors (i.e., family history of hypertension), and that weight control during pregnancy is more important for the patients with mild preeclampsia.

When dividing preeclampsia patients into four groups according to parity and onset of disease, we demonstrated that primiparae group complicated with early onset was the most severe among these four groups. Such results as the early termination (36.9±0.5 wk) and the significantly low birth weight (1599±871 kg) may reflect the high incidence of severe preeclampsia in primiparae with early onset. Thus, it is thought that the estimation of fetal body weight is a useful indicator to determine the severity of disease. On the contrary, our results implied that the group of multiparae with late onset of preeclampsia was the mildest one, because of the lowest frequency of severe preeclampsia and the rate of cesarean section.

Moreover, in order to elucidate the factors that affected mode of delivery, we examined the following data: maternal age, family history of hypertension, the incidence of severe preeclampsia and IUGR, birth weight and placental weight. There was a significant low birth weight and placental weight in the patients who underwent cesarean section compared with those who had vaginal delivery. Therefore, we confirmed that the patients with low birth weight and low placental weight were at increased risk for cesarean section.

In conclusion, we found that maternal characteristics of preeclamptic patients (including age, parity and family history), onset of disease and fetal growth were important parameters for the prediction of the severity of preeclampsia and incidence of IUGR and mode of delivery.

Acknowledgments

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