IgA Nephropathy and Pregnancy

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In the present study, we investigated the pregnancy course of 60 pregnant women with IgA nephropathy according to the grade of nephropathy. All the patients had undergone open renal biopsy at the Renal Metabolism Unit, Department of Internal Medicine, Tokai University Hospital, before pregnancy. The items analyzed were the serum biochemical data, the occurrence and severity of EPH-gestosis, the frequency of low birth weight infants, and the incidence of intrauterine growth retardation (IUGR).

Analysis of the serum biochemical data revealed no statistically significant differences among the various grades.

Investigating the occurrence and severity of EPH-gestosis revealed that the incidence was 0.0% in patients of grade I (n=7), 56.1% for mild EPH-gestosis and 22.0% for severe EPH-gestosis in those of grade II (n=41), 45.5% for mild EPH-gestosis and 18.2% for severe EPH-gestosis in those of grade III (n=11), and 0.0% in those of grade IV (n=1). These results showed statistically significant differences in the incidence of EPH-gestosis according to the grade.

Analyzing the frequency of low birth weight infants (less than 2,500g at birth) showed rates of 28.6% for grade I, 17.1% for grade II, 36.4% for grade III, and 100.0% for grade IV. No statistically significant differences were observed.

The incidence of IUGR was 0.0% for grade I, 9.8% for grade II, 18.2% for grade III, and 0.0% for grade IV, indicating no statistically significant differences.

Therefore, we concluded that in pregnancy complicated with IgA nephropathy, if the renal function before pregnancy was satisfactory, an uneventful course of pregnancy could be expected by careful control of the patients, although the incidence of EPH-gestosis was high.

Key Words: IgA nephropathy, pregnancy, EPH-gestosis, IUGR

INTRODUCTION

IgA nephropathy, the most frequent among the diseases of primary chronic glomerulonephritis, has a peak onset age coinciding with the reproductive age. This often raises an issue that this disease easily becomes a complication during pregnancy (1, 2, 3, 4).

According to various reports (5, 6), a normal course of pregnancy can be anticipated in pregnant women with IgA nephropathy and the renal function will not be affected adversely after delivery if they have a glomerular filtration rate (GFR) of more than 70 ml/min before pregnancy as well as normal blood pressure. It has been assumed that the incidence of EPH-gestosis (7), IUGR (8), abortion (7), fetal death (7), and impairment of renal function after delivery (7, 9) is significantly high in patients with a GFR of less than 50 ml/min and a serum creatinine level of more than 1.4mg/dl.

In the present study, we classified 60 patients, who underwent open renal biopsy at the Renal Metabolism Unit, Department of Internal Medicine, Tokai University Hospital before pregnancy, and were diagnosed as having IgA nephropathy; into grades I to IV, according to the classification by Nomoto et al (10). We analyzed the course of pregnancy and delivery of the individual patients, particularly focusing on the relations of pregnancy complicated by IgA nephropathy to EPH-gestosis and IUGR.

SUBJECTS AND METHODS

1. Subjects

abbreviations
EPH ; edema, proteinuria, hypertension. IUGR ; intrauterine, growth, retardation.
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The subjects were 60 pregnant women with IgA nephropathy who delivered at our hospital between January 1981 and December 1995. All the patients had undergone open renal biopsy at the Renal Metabolism Unit, Department of Internal Medicine of our hospital before pregnancy and were diagnosed as having IgA nephropathy of various grades.

There were 7 patients in grade I, 41 in grade II, 11 in grade III, and 1 in grade IV (Fig. 1).

In addition, excluding one patient with grade IV IgA nephropathy, pregnancy was allowed in all the patients because of satisfactory control of IgA nephropathy before pregnancy.

2. Pathological classification (Fig. 2, Table 1)

The patients were classified as follows according to the classification of Nomoto et al (10).

(1) Grade I (minimal stage)
Presence of minimal focal segmental thickening of mesangial areas.

(2) Grade II (slight stage)
Presence of diffuse mesangial thickening

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**Fig. 1** The list of 60 cases of the pregnancy complicated with IgA nephropathy

**Fig. 2** Histopathological change of IgA Nephropathy
with an increase in the homogeneous PAS-positive mesangial matrix and mild and segmental hypercellularity.

(3) Grade III (moderate stage)
Presence of diffuse mesangial thickening and mesangial proliferation.

(4) Grade IV (advanced stage)
Presence of marked capsular adhesion, fibrocellular crescents, glomerular hynalnosis and sclerosis.

3. Assessment of renal function
BUN, serum creatinine and uric acid levels, which are relatively less affected by pregnancy and are characteristic to EPH-gestosis, were used as the parameters.

4. Evaluation of the course of pregnancy (presence of or absence of EPH-gestosis)
The course of pregnancy was evaluated by the occurrence and severity of EPH-gestosis, which has a close relationship with the pregnancy-associated renal diseases. The evaluation was made according to the criteria set by the Committee of EPH-gestosis of the Japanese Society of Obstetrics and Gynecology.

5. Evaluation of IUGR
Those showing a value lower than \(-1.5\) S. D. on the fetal growth curve by Nishida et al. (11) were evaluated as IUGR.

RESULTS

1. Laboratory data
Table 2 lists BUN, serum creatinine and uric acid levels by the grade of IgA nephropathy throughout the course of pregnancy. No statistically significant differences were found between the grades I, II and III. The statistical analysis was made by the unpaired t-test. Although pregnancy is normally prohibited in grade IV patients, one patient of grade IV was already at the 29th week of gestation when she visited our hospital. At that time, because an abnormally high serum creatinine level of 9.0 mg/dl was detected, emergency cesarean sec-

Table 1 Histopathological classification of IgA Nephropathy (by Nomoto et al.)

| Grade (I) | minimal | : minimal focal segmental thickening of mesangial areas. |
| Grade (II) | slight | : diffuse mesangial thickening with an increase in the homogeneous PAS-positive mesangial matrix. mild and segmental hypercellularity. |
| Grade (III) | moderate | : diffuse mesangial thickening and mesangial proliferation. |
| Grade (IV) | advanced | : marked capsular adhesion, fibrocellular crescents, glomerular hynalnosis and sclerosis. |

Table 2 Relationship between Renal Function and IgA Nephropathy

<table>
<thead>
<tr>
<th>Grade</th>
<th>Cases</th>
<th>BUN*</th>
<th>Creatinine*</th>
<th>UA*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>max</td>
<td>min</td>
<td>mean</td>
</tr>
<tr>
<td>I</td>
<td>7</td>
<td>12.2</td>
<td>6.0</td>
<td>6.0</td>
</tr>
<tr>
<td>II</td>
<td>37</td>
<td>12.9</td>
<td>12.0</td>
<td>0.7</td>
</tr>
<tr>
<td>III</td>
<td>11</td>
<td>12.9</td>
<td>1.0</td>
<td>0.7</td>
</tr>
<tr>
<td>IV</td>
<td>1</td>
<td>45.0</td>
<td></td>
<td>9.0</td>
</tr>
</tbody>
</table>

*mg/ dl

Table 3 Relationship between EPH and IgA Nephropathy

<table>
<thead>
<tr>
<th>Grade</th>
<th>Cases</th>
<th>Number of mild EPH</th>
<th>Number of severe EPH</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>II</td>
<td>41</td>
<td>(0.0%)</td>
<td>(0.0%)</td>
<td>(100.0%)</td>
</tr>
<tr>
<td>III</td>
<td>11</td>
<td>(56.1%)</td>
<td>(22.0%)</td>
<td>(22.0%)</td>
</tr>
<tr>
<td>IV</td>
<td>1</td>
<td>(45.5%)</td>
<td>(18.2%)</td>
<td>(36.4%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of mild EPH</th>
<th>Number of severe EPH</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>(0.0%)</td>
<td>(0.0%)</td>
<td>(100.0%)</td>
</tr>
</tbody>
</table>
tion was performed.

2. Course of pregnancy (occurrence and severity of EPH-gestosis)

Table 3 shows the incidence of EPH-gestosis throughout the course of pregnancy. None of the patients of grade I developed EPH-gestosis (0.0%, 0/7). In patients of grade II, mild EPH-gestosis occurred in 23/41 (56.1%) and severe EPH-gestosis in 9/41 (22.0%). On the other hand, in patients of grade III, mild EPH-gestosis occurred in 5/11 (45.5%) and severe EPH-gestosis in 2/11 (18.2%). Statistically, significant differences were observed between grade I and grade II and between grade I and grade III regarding the incidence of EPH-gestosis (p<0.01) and the severity of EPH-gestosis (mild and severe) (p<0.05), but there were no significant differences between grade II and grade III in both parameters. The statistical analysis was performed using Kruskal-Wallis test.

In one patient of grade IV, no findings of EPH-gestosis were identified at the time of consultation. This may be because she was receiving continuous ambulatory peritoneal dialysis (CAPD).

Table 4 lists the incidence (expressed as %) of edema, proteinuria and hypertension at 3 different stages of pregnancy. It is seen at first glance that there were so many patients with proteinuria. Investigating proteinuria, demonstrated that three patients of grade II had proteinuria severe in the 1st trimester; one then had intraterine fetal death, the second developed fetal distress, and the third one had an uneventful course of pregnancy. The frequency of mild proteinuria increased as the stage of pregnancy advanced in both groups of grade II and grade III.

The study of blood pressure revealed that one patient of grade II with hypertension severe in the 1st trimester underwent cesarean section at 34 weeks and 4 days of gestation due to diagnosis of fetal distress and IUGR. The

<table>
<thead>
<tr>
<th>Table 4 Rate of EPH during Pregnancy (%)</th>
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<tbody>
<tr>
<td>Grade</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>II</td>
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<tr>
<td></td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>IV</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

Fig. 3 Birth weight of the pregnancy complicated with IgA nephropathy (1)
neonate weighed 1,560g. When grade II was compared with grade III, the course of hypertension was better in grade III than in grade II.

3. Analysis of birth weight

Figure 3 shows a diagram obtained by plotting the birth weight and gestational age (weeks) in the respective grade groups of IgA nephropathy. There was a statistically significant correlation between the birth weight and the gestational age in all the pregnancies associated with IgA nephropathy (correlation coefficient= 0.75, p<0.001). The correlation was analyzed using Pearson’s correlation coefficient.

Figure 4 shows the mean birth weight in each group (mean±S. D.). No statistically significant differences were found between grades I, II and III. The statistical analysis was performed using unpaired t-test.

Table 5 displays the rate of low birth weight infants (weighing less than 2,500g at birth), the mean birth weight, S. D. value vs. fetal growth curve by Nishida et al. (11), and the frequency of IUGR in each grade group. Despite absence of any statistically significant differences between the grades, there was a tendency of a greater frequency of IUGR for grade III than for grade II. Statistically, the rate of low birth weight infants and the frequency of IUGR were assayed using Kruskal-Wallis test, and the birth weight and S. D. were analyzed using the unpaired t-test.

**DISCUSSION**

The above results are summarized in Table 6. In managing pregnant women having associated renal diseases, it is important to set standardized criteria to permit continuation of pregnancy in order to expect uneventful course of pregnancy in the future. In general, whether or not pregnancy can be continued is determined according to the guidelines of the Japanese Ministry of Health and Welfare or criteria of Amagasaki et al. (12). More specifically, it has been assumed that an uneventful pregnant course can be expected in those with a GFR value of more than 70 ml/dl, a serum creatinine level of less than 1.1 mg/dl, and a blood pressure of less than 140/90 mmHg. In

![Birth Weight of the Pregnancy Complicated with IgA Nephropathy](image)

**Table 5** Relationship between Birth Weight, IUGR and IgA Nephropathy

<table>
<thead>
<tr>
<th>Grade</th>
<th>Cases</th>
<th>Number of Low Birth Weight</th>
<th>Average Birth Weight (g)</th>
<th>S. D. vs. Fetal Growth Curve</th>
<th>Number of IUGR</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>7</td>
<td>2 (28.6%)</td>
<td>2649.1</td>
<td>-0.47</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>II</td>
<td>41</td>
<td>7 (17.1%)</td>
<td>2863.4</td>
<td>-0.39</td>
<td>4 (9.8%)</td>
</tr>
<tr>
<td>III</td>
<td>11</td>
<td>4 (36.4%)</td>
<td>2590.1</td>
<td>-1.07</td>
<td>2 (18.2%)</td>
</tr>
<tr>
<td>IV</td>
<td>1</td>
<td>1 (100.0%)</td>
<td>1180</td>
<td>-1.32</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>
the present study, we investigated 59 pregnant women having IgA nephropathy of grade I to III who permitted to conceive and to continue pregnancy and their pregnancies were successful for more than 22 weeks, and one patient with IgA nephropathy of grade IV who continued pregnancy without any permission of pregnancy. These subjects were selected from those diagnosed by open renal biopsy before pregnancy as having IgA nephropathy.

The incidence of EPH-gestosis increases as the grade of IgA nephropathy advances. In our present results, the incidence was 78.1% in the patients of grade II and 63.6% in the patients of grade III. Considering the fact that the incidence of pure EPH-gestosis is about 10% in Japan, we think that our result is abnormally high. If nephropathy is controlled adequately and satisfactorily, more than 70% of patients can continue pregnancy in a state of mild and moderate nephropathy. This suggests the significance of counseling and control of pregnant women. In more than 50% of the Japanese pregnant women, the symptoms of EPH-gestosis is edema. In the present study, however, it was found that IgA nephropathy-associated EPH-gestosis is characterized by proteinuria.

With respect to IUGR, there was no difference in the incidence between the grades of IgA nephropathy, but the overall incidence was 10% (6/60). From the fact that the incidence of IUGR is about 5% in the Japanese nationwide statistics of total pregnancies, the incidence of 10% obtained in the present analysis of pregnancies associated with IgA nephropathy is larger than the value in the normal group. However, there were practically no serious problems in the fetal development, for example, severe fetal distress or abnormal amniotic fluid during the prenatal control.

Furthermore, we analyzed the frequency of low birth weight infants weighing less than 2,500g at birth. The overall frequency was 23.3% in all the pregnancies associated with IgA nephropathy. Whereas, the frequency of low birth weight infants is about 10% in the Japanese nationwide statistics of all pregnancies. The frequency of 23.3% in our present analysis is higher that the value of normal group. This may be because the incidence of mixed EPH-gestosis was relatively high in patients with IgA nephropathy in whom continuation of pregnancy was judged as possible, and because termination of pregnancy was forced in certain patients.

In the present study, we investigated, at Tokai University Hospital, the course of pregnancy, the incidence of EPH-gestosis, and the frequency of IUGR in pregnant women having IgA nephropathy of grades I to III according to the classification by Nomoto et al. From the results, we think that patients with a renal function within the normal range and free from hypertension can continue pregnancy rather satisfactorily and can deliver healthy infants if the development of EPH-gestosis is well prevented mainly by dietary instruction and ordinary life counseling during pregnancy. It is also intended in the future to make every effort to control pregnant women, aiming at development of a new technique that enables prediction of possible future development of

<table>
<thead>
<tr>
<th>Grade</th>
<th>Cases</th>
<th>EPH</th>
<th>IUGR</th>
<th>Low Birth Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>mild</td>
<td>severe</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>7</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>41</td>
<td>23</td>
<td>9</td>
<td>4</td>
</tr>
<tr>
<td>III</td>
<td>11</td>
<td>5</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>IV</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>total</td>
<td>60</td>
<td>28</td>
<td>11</td>
<td>6</td>
</tr>
</tbody>
</table>

Table 6 Summary; Relationship between EPH, IUGR, Low Birth Weight and IgA Nephropathy
EPH-gestosis at the early stage of pregnancy.
A summary of this paper was presented at
the 15th FIGO World Congress of Gynecology
and Obstetrics.

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