ORIGINAL ARTICLE

Diagnosis and management of fetal growth restriction and uteroplacental dysfunction in hypertensive disorders of pregnancy in Japan: a nationwide survey by the Japan Society for the Study of Hypertension in Pregnancy (JSSHP)

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Aim: The definition and classification of hypertensive disorders of pregnancy were revised in 2018. This study aimed to evaluate the degree to which the new definition (especially that of uteroplacental dysfunction) was accepted and understood by Japanese obstetricians for the two years immediately following the revision (2018–2020).

Methods: The scientific committee of the Japan Society for the Study of Hypertension in Pregnancy (JSSHP) surveyed the current state of the diagnosis and management of uteroplacental dysfunction in hypertensive disorders of pregnancy. An online, anonymous questionnaire was distributed to 625 JSSHP members via Research Electronic Data Capture (REDCap) software in February 2020.

Results: Valid responses were obtained from 147 obstetricians. In normal pregnancies, 75% of obstetricians measured fetal growth at each visit, and the frequency of uteroplacental dysfunction increased in the order of chronic hypertension, gestational hypertension, and preeclampsia. Approximately 70% of obstetricians accepted uteroplacental dysfunction as a preeclampsia diagnostic criterion. The majority included fetal growth restriction when diagnosing uteroplacental dysfunction, but there was wide variation among obstetricians who included findings other than FGR (such as abnormal umbilical artery Doppler flow and stillbirth). Although uteroplacental dysfunction was frequently the reason for admission, criteria for determining pregnancy termination varied widely.

Conclusions: In Japan, frequent ultrasonography is performed to diagnose uteroplacental dysfunction. Many obstetricians include uteroplacental dysfunction as a diagnostic criterion for preeclampsia, and these patients are carefully managed. However, there is wide variation in diagnostic criteria and management policies.

Introduction

The definition and classification of hypertensive disorders of pregnancy (HDP) were revised in 2018 by the Japan Society for the Study of Hypertension in Pregnancy (JSSHP) and the Japan Society of Obstetrics and Gynecology.¹⁾ Preeclampsia (PE) was conventionally diagnosed when there was proteinuria in hypertension after 20 weeks of gestation. However, with the new definition, PE is diagnosed when hypertension is associated with other types of maternal organ dysfunction or uteroplacental dysfunction, even in the absence of proteinuria. This new definition is appropriate given the etiology and pathophysiology of PE and is consistent with international guidelines.^{2–5)} However, the definitions in each guideline slightly differ, for example, with regard to the presence of maternal organ dysfunction and uteroplacental dysfunction.

The International Society for the Study of Hypertension in Pregnancy (ISSHP) defines fetal growth restriction (FGR) as a consequence of uteroplacental dysfunction as a PE diagnostic criterion, as does the JSSHP.²⁾ Uteroplacental dysfunction includes FGR (generally defined as an estimated fetal weight of -1.5 standard deviations (SD) or less in Japan), presence of abnormal umbilical artery Doppler wave flow, and stillbirth. Uteroplacental dysfunction is also one of the severe criteria for PE.¹⁾ However, there is little evidence regarding the effect of adopting the new definition on perinatal outcomes, and changes to the management strategy have not been established.^{6–12)} Different standards are used for diagnosing FGR and uteroplacental dysfunction in each country, and different obstetricians follow different management protocols.¹³⁾

The present nationwide survey aimed to 1) clarify how Japanese obstetricians diagnose FGR or uteroplacental dysfunction and manage patients with HDP in Japan and 2) evaluate the degree to which the new definition (especially that of uteroplacental dysfunction) was accepted and understood by Japanese obstetricians during the two years immediately following the revision (2018–2020).

Materials and methods

Anonymous self-administered questionnaires were distributed to 625 members of the JSSHP. Study data were collected from February 18, 2020, to May 15, 2020, using Research Electronic Data Capture (REDCap) software. Questions were asked regarding respondent characteristics, the frequency of fetal growth measurement, FGR and uteroplacental dysfunction diagnoses, diagnostic criteria used, and the management strategy for uteroplacental dysfunction in HDP

(Supplementary file). Results are presented as numbers and percentages. The present study was approved by the Institutional Ethics Committee of Osaka University (approval number: 19326). JSSHP members provided consent to participate in the study by checking off a box on the answer sheet.

Results

Respondent characteristics

Responses were received from 169 of 625 JSSHP members, of whom 149 were obstetricians (88.2%) and 20 were not (11.8%). Two questionnaires were excluded due to insufficient responses; hence, a total of 147 questionnaires from obstetricians were analyzed. The median age was 49 years (range: 29–84). Affiliation distributions were as follows: general perinatal medical centers (41.0%), regional perinatal centers (38.5%), general hospitals (8.3%), and clinics (9.6%).

Fetal growth monitoring frequency

Approximately 75% of obstetricians measured fetal growth at each medical visit, even in normal pregnancies, throughout the antenatal period (Figure 1A). In patients with suspected FGR, approximately 80% of obstetricians measured fetal growth parameters weekly or more frequently (Figure 1B). Approximately 70% of respondents measured fetal growth parameters every two weeks for patients with chronic hypertension (CH) (Figure 1C), and approximately 40% measured fetal growth weekly or more frequently for patients with gestational hypertension (GH) (Figure 1D). For patients with PE, 80% of respondents measured fetal growth parameters weekly or more frequently, similar to FGR (Figure 1E).

Diagnosis of FGR and uteroplacental dysfunction

Most respondents used an estimated fetal weight criterion of -1.5 SD or less to diagnose FGR. Approximately 25% of obstetricians used other criteria, but most diagnosed FGR based solely on estimated fetal weight (Figure 2A). More than 80% of obstetricians performed ultrasound examinations of amniotic fluid volume and Doppler imaging at each visit to assess the well-being of the fetus (Figure 2B). Regarding the question of whether to include uteroplacental dysfunction in PE criteria or not, 69% answered “Yes,” which increased to 80% when the answer “Will be included in the future” was included (Figure 2C). Most diagnostic criteria for uteroplacental dysfunction included FGR, but other criteria varied widely (Figure 2D). For CH, 55% answered “Yes” to the question of including uteroplacental dysfunction in superimposed preeclampsia (SPE) criteria (Figure 2E), and 63% answered “Yes” to the question of including

Figure 1. Ultrasound examination frequency for estimating fetal weight.

A: Normal pregnancy. B: Pregnancy with FGR. C: Pregnancy with CH. D: Pregnancy with GH. E: Pregnancy with PE. FGR, fetal growth restriction; CH, chronic hypertension; GH, gestational hypertension; PE, preeclampsia.

uteroplacental dysfunction in severe criteria for PE. However, this increased to almost 80% when the answer “Will be included in the future” was included (Figure 2F).

FGR and uteroplacental dysfunction management and hospitalization

Most obstetricians hospitalized patients for FGR, including those who answered “Occasionally” (Figure 3A). More than 60% stated that the reasons for hospitalization were FGR severity, oligohydramnios, non-reassuring fetal status (NRFS), and abnormal Doppler imaging (Figure 3B). More than 80% answered that if HDP accompanied FGR, they would adjust the management strategy (Figure 3C). Most respondents also answered that they hospitalized patients if CH or GH accompanied uteroplacental dysfunction (Figure 3D).

Pregnancy termination for FGR and uteroplacental dysfunction

Abnormalities at the fetal well-being assessment were the most common reason for FGR pregnancy termination (90%), followed by maternal complications and growth arrest. Less than 60% of obstetricians used gestational weeks as a criterion (Figure 4A). Criteria for deciding when to terminate pregnancy with FGR based only on gestational weeks differed substantially among obstetricians (Figure 4B). Obstetricians answered similarly about the timing of delivery when HDP was complicated by uteroplacental dysfunction (34 weeks or 37 weeks), but the majority answered that the basis for the decision was not clear (Figure 4C).

A survey of uteroplacental dysfunction

A

B

C

D

Figure 2. Diagnosis of FGR and uteroplacental dysfunction.

A: FGR diagnostic criteria. B: The method for evaluating fetal well-being at each visit in pregnancies with FGR. C: The percentage who responded that uteroplacental dysfunction is included in the PE diagnostic criteria. D: Uteroplacental dysfunction diagnostic criteria (only including those who answered “Yes” in 2C). E: The percentage who responded that uteroplacental dysfunction is included in the PE diagnostic criteria for CH. F: The percentage who responded that uteroplacental dysfunction is included in the PE severity criteria.

FGR, fetal growth restriction; AF, amniotic fluid; BPS, biophysical profile score; NST, non-stress test; PE, preeclampsia; NRFS, non-reassuring fetal status; UmA, umbilical cord artery; IUFD, intrauterine fetal death; CH, chronic hypertension. The number next to the bar chart represents the number of respondents.

Discussion

The present survey identified an almost unified FGR diagnostic criterion (fetal weight of -1.5 SD or less), and ultrasonography examinations were frequently performed to identify FGR and evaluate the well-being of the fetus. However, management strategies varied widely. Diagnostic criteria and management policies also varied widely with respect to uteroplacental dysfunction in HDP. However, many obstetricians included uteroplacental dysfunction as a PE diagnostic criterion, which was then carefully managed.

Fetal growth measurement frequency

For most normal pregnancies, Japanese obstetricians perform fetal growth measurement at each medical visit. Fetal growth measurement is the most common way that FGR is identified, but is prone to large errors, and it is unclear if frequent measurement contributes to an improved prognosis. The American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin also recommends fetal growth measurement every 3–4 weeks for FGR.¹⁴⁾ The increased frequency of fetal growth measurement with CH, GH, and PE suggests that many obstetricians believe the pathology of these conditions is closely related to FGR. Most obstetricians answered that FGR was used to diagnose uteroplacental dysfunction in PE, and 84% answered that if PE accompanied FGR, they would adjust their management strategy. The ISSHP guidelines recommend fetal growth measurement every two to four weeks for patients with

CH after 26 weeks and every two weeks for patients with PE.²⁾ The ACOG recommends measurements at least once in the third trimester for patients with CH¹⁵⁾ and every three to four weeks for patients with GH or PE, the same as for FGR.³⁾ The National Institute for Health and Care Excellence (United Kingdom) guidelines recommend measurements at 28, 32, and 36 weeks of gestation for patients with CH, every two to four weeks for patients with GH, and every two weeks for patients with PE or severe GH.⁴⁾

Diagnosis of FGR and uteroplacental dysfunction

In Japan, the FGR diagnostic criterion is an estimated fetal weight of -1.5 SD or less,¹⁶⁾ and many obstetricians answered that this is the criterion they use. The majority responded that they diagnose FGR only by estimated fetal weight, but 25% answered that they use additional information. FGR diagnoses are not unified among obstetricians, as the diagnosis may include constitutionally small infants. According to the International Society of Ultrasound in Obstetrics and Gynecology, small infants less than the third percentile are diagnosed as FGR only by estimating fetal weight, but beyond that, a diagnosis should be made by referring to fetal growth rate and umbilical artery blood flow.¹⁷⁾ An increasing number of obstetricians answered that the diagnosis of uteroplacental dysfunction includes findings other than FGR. However, whether or not FGR is included in the PE definition also depends on national guidelines. FGR is included in the PE diagnosis guidelines of ISSHP and the Society of Obstetric Medicine of Australia and New

A survey of uteroplacental dysfunction

A

B

C

D

Figure 3. FGR and uteroplacental dysfunction management.

A: The percentage of respondents who would hospitalize patients for FGR. B: The reason for hospitalization for FGR (only including those who answered “Often” in 3A). C: The percentage who would change management strategies when FGR is complicated with HDP. D: The percentage who would hospitalize patients when uteroplacental dysfunction is complicated with CH or GH (only for those who answered “Yes” in 2C or E).

FGR, fetal growth restriction; HDP, hypertensive disorders of pregnancy; CH, chronic hypertension; GH, gestational hypertension.

The number next to the bar chart represents the number of respondents.

Figure 4. Pregnancy termination for FGR.

A: Factors used to determine pregnancy termination for FGR. B: Gestational weeks for pregnancy termination with FGR (only for those who answered “Gestational weeks” in 4A). C: Gestational weeks for pregnancy termination when uteroplacental dysfunction is complicated with preeclampsia.

FGR, fetal growth restriction.

The number next to the bar chart represents the number of respondents.

Zealand (SOMANZ).^{2,5)} The ACOG included FGR in the definition in 2002,¹⁸⁾ but it was omitted in 2020³⁾ because the FGR diagnosis is not unified, difficult to make, and not always related to PE pathology. ISSHP and SOMANZ also state that SPE is not diagnosed when there is CH and FGR^{2,5)} because CH is accompanied by FGR in 25% of cases.²⁾

FGR and uteroplacental dysfunction management and hospitalization

Most obstetricians hospitalized patients with FGR, suggesting that hospitalization is relatively common for FGR management, even without PE. The reasons for hospitalization were severe FGR, oligohydramnios, NRFS, and abnormal Doppler imaging, accounting for more than 60% of all answers, implying that the management policy changed based on severity, rather than solely on FGR. For PE, each country’s guidelines recommend

hospitalization when there are severe symptoms.^{2–5)} In our study, more than 80% of respondents answered that they would change some management strategies if PE accompanies FGR. The incidence of placental abruption is 1% in women with PE without FGR, but this increases to 9.8% in PE with FGR.⁷⁾ In Japan, hospitalization management is recommended for PE in principle, suggesting that more strict management is required when PE accompanies FGR. When CH or GH accompanies uteroplacental dysfunction, most respondents answered that the patients would be hospitalized, also reflecting the situation in Japan where patients with PE are hospitalized in principle.

Pregnancy termination for FGR and uteroplacental dysfunction

Most international guidelines agree that women with PE should consider delivery beyond 37+0 gestational

weeks.^{2–5)} However, the timing of FGR pregnancy termination should be considered situationally and there is no international consensus, which was also reflected in this survey. In the ACOG guidelines, FGR was excluded from the PE severity criteria. Thus, it is not an indication for pregnancy termination with PE.³⁾ However, the guidelines state that delivery should be considered after 34 gestational weeks if there are complications such as hypertension in FGR,¹⁴⁾ but this recommendation is not stated in the ISSHP guidelines.²⁾ Furthermore, in this survey, we did not investigate the timing of termination of pregnancy when FGR is associated with either CH or GH. Further investigation will be needed for these conditions as well.

Limitations

This study has some limitations. First, the response rate was not high, with only about 27% responding to the survey. Second, this questionnaire was sent only to JSSHP members. Therefore, the results mainly reflected the opinions of obstetricians belonging to perinatal centers and may not reflect the current practices of general obstetricians throughout Japan.

Conclusion

FGR was diagnosed by frequent ultrasound examinations, and many obstetricians included uteroplacental dysfunction as a PE diagnostic criterion, which was then managed very carefully. However, there were large variations in uteroplacental dysfunction diagnostic criteria and management strategies. The present findings suggest that the new definition was not always widely accepted and understood by obstetricians. Further research should be conducted to determine if the new definition is scientifically valid, if uteroplacental dysfunction is a suitable diagnostic criterion of PE in the case of non-proteinuric HDP, and if other FGR criteria such as an abnormal umbilical artery blood flow should be included.

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Conflicts of interest

The authors declare that they have no competing interests.

Informed consent for reporting

Informed consent was obtained from the obstetricians completing the survey.

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Supplementary file on original questionnaire of this study

Ultrasound examination frequency for estimating fetal weight.

Q1. How often are fetal ultrasound measurements performed at regular maternity visits?

1. Every medical visit
2. Every 2 weeks
3. Every 4 weeks
4. About 3 times throughout the maternity visits
5. Others

Q2. How often are fetal ultrasound measurements performed in pregnancy with fetal growth restriction (FGR)?

1. Every 1 week or more
2. Every 2 weeks
3. Every 3 weeks
4. Every 4 weeks
5. Others

Q3. How often are fetal ultrasound measurements performed in pregnancy with chronic hypertension (CH)?

1. Every 1 week or more
2. Every 2 weeks
3. Every 3 weeks
4. Every 4 weeks
5. Others

Q4. How often are fetal ultrasound measurements performed in pregnancy with gestational hypertension (GH)?

1. Every 1 week or more
2. Every 2 weeks
3. Every 3 weeks
4. Every 4 weeks
5. Others

Q5. How often are fetal ultrasound measurements performed in pregnancy with preeclampsia (PE)?

1. Every 1 week or more
2. Every 2 weeks
3. Every 3 weeks
4. Every 4 weeks
5. Others

FGR and uteroplacental dysfunction diagnosis.

Q6. What are the criteria needed to diagnose FGR? (Multiple selections are possible)

1. Estimated fetal weight is -1.5 standard deviations or less based on the Japanese standard using ultrasonography data
2. Estimated fetal weight is less than the 10th percentile

3. Those without chromosomal abnormalities or fetal structural anomalies

4. Diagnosis is based not only on the estimated fetal weight but also on other findings

5. Others

Q7. What tests are performed at each visit to assess well-being of FGR? (Multiple selections are possible)

1. Amniotic fluid volume
2. Biophysical profile score
3. Non-stress test
4. Contraction stress test
5. Fetal Doppler imaging
6. Others

Q8. Is uteroplacental dysfunction included in diagnostic criteria for PE?

1. Yes
2. No
3. Will be included in the future
4. Others

Q9. (Only for those who answered 1 in Q8) What are the criteria for uteroplacental dysfunction in the diagnosis for PE? (Multiple selections are possible)

1. FGR
2. Oligohydramnios
3. Non-reassuring fetal status
4. Umbilical artery Doppler abnormality
5. Intrauterine fetal death
6. Others

Q10. Is uteroplacental dysfunction included in the diagnostic criteria for superimposed PE of pregnancy with CH?

1. Yes
2. No
3. Will be included in the future
4. Others

Q11. Is uteroplacental dysfunction included in the diagnostic criteria as “severe” of hypertensive disorders of pregnancy (HDP)?

1. Yes
2. No
3. Will be included in the future
4. Others

FGR and uteroplacental dysfunction management and hospitalization.

Q12. Are pregnant women with FGR hospitalized for purposes other than delivery?

1. Often
2. Occasionally
3. Rarely
4. Others

Q13. (Only for those who answered 1 in Q12) What is the reason for hospitalization of pregnant women with FGR? (Multiple selections are possible)

1. Severity of FGR
2. Oligohydramnios
3. Fetal Doppler abnormality
4. Fetal heart rate abnormality
5. Fetal growth arrest
6. Others

Q14. Does the management strategy change if HDP accompanies FGR?

1. Yes
2. No
3. Others

Q15. (Only for those who answered 1 in Q8 or Q10) Are pregnant women hospitalized if CH or GH accompanies uteroplacental dysfunction?

1. Yes
2. No
3. Will be Yes in the future
4. Others

Pregnancy termination for FGR.

Q16. What are the factors used to determine the pregnancy termination for FGR? (Multiple selections are possible)

1. Gestational week
2. Fetal well-being assessment
3. Fetal growth arrest
4. Maternal comorbidity (hypertension, etc.)
5. Others

Q17. (Only for those who answered 1 in Q16) How many weeks of gestation does the pregnancy termination for FGR determine in the absence of exacerbation with fetal well-being or maternal comorbidity?

1. 37 weeks
2. 38 weeks
3. 39 weeks
4. After 40 weeks
5. Others

Q18. How many weeks of gestation does the pregnancy termination determine in the presence of uteroplacental dysfunction with HDP?

1. Before 34 weeks
2. 34 weeks
3. 37 weeks
4. No particular standard
5. Others