Title: The association between chronic deciduitis and preeclampsia.

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Highlights

・Preeclampsia is frequently found in pregnants with chronic deciduitis.

・Chronic deciduitis is frequently found in pregnants with preeclamsia.

・Chronic deciduitis is related to poor perinatal outcomes.

Key words: chronic deciduitis, chronic endometritis, hypertensive disorders of

pregnancy, perinatal outcomes, preeclampsia

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Ethics statement:

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page. This research was approved by the Ethics Committee of Shiga University of Medical Science (R2020-074). The information on conducting the study was made public, and the opportunity for refusal was guaranteed as much as possible by optout as the Ethics Committee suggested.

Abstract

Chronic deciduitis (CD) is slight inflammation of the decidua found during pregnancy. The cause of preeclampsia is thought to be placental hypoplasia, and various theories have been proposed to explain the detailed mechanism; however, its association with decidual inflammation is unclear. A retrospective case control study was conducted in a single university. Subjects were cases who delivered by cesarean section between January 1, 2013 and June 30, 2020 and whose placentas were pathological assessed. CD was diagnosed by CD138 immunostaining of placental decidua tissue, and the perinatal prognosis and incidences of hypertensive disorder of pregnancy (HDP) and preeclmpsia were examined according to the presence or absence of CD. A logistic regression analysis was performed to evaluate the association between preeclampsia and 11 explanatory variables (10 patient or perinatal background factors and CD). The study population included 76 patients (non-CD, n=54; CD, n=22). The rate of preeclampsia was significantly higher in the CD group (P=0.0006). Patients with CD gave birth at a significantly earlier gestational age (P=0.040) with a lower birth weight (P=0.001), and a higher rate of LFD (P=0.005). The Apgar scores at 1 and 5 minutes and umbilical artery pH were lower (P=0.0003, 0.021 and 0.002, respectively) in the CD group. The logistic regression analysis revealed that CD was positively associated with preeclampsia. A retrospective examination of the placenta found that patients with CD had a significantly higher incidence of preeclampsia and CD is considered to be a factor that is associated with poor perinatal outcomes.

Main text

1. Introduction

Chronic deciduitis (CD) is a type of long-term slight inflammation of the decidua that occurs during pregnancy (Khong et al., 2000) (Kim et al., 2015). Chronic microbial infection or immune mechanisms have been implicated in the etiology of CD (Kim et al., 2015), although the details of its pathophysiology remain unknown. CD is histologically diagnosed based on the presence of lymphocytes and plasma cells in the decidua(Khong et al., 2000) (Kimura et al., 2019) (Maroun et al., 2014). In particular, it has been reported that infiltration of plasma cells into the decidua results in a high severity of CD and is highly diagnostic for CD (Khong et al., 2000). CD is infrequently noticed by clinicians because it is histologically diagnosed using the removed placenta, but it can affect immunity and influence the establishment and maintenance of pregnancy. In fact, recent reports have revealed that CD is associated with miscarriage (Kaku et al., 2020), fetal growth restriction (Bendon and Miller, 1990), fetal death (Bendon and Miller, 1990), and preterm labor (Edmondson et al., 2009).

Hypertensive disorders of pregnancy (HDP) is a disease that causes hypertension, proteinuria and organ damage in pregnant women and results in preterm birth and fetal growth restriction, resulting in a poor perinatal prognosis for both the pregnant woman and newborn. Abnormal placentation is considered a major cause of HDP, especially preeclampsia. However, the detailed mechanism underlying abnormal placentation has not been clarified, although many theories, including oxidative stress, immunity, infection, genetic and environmental factors (Brown et al., 2018) (Burton et al., 2019) (Geldenhuys et al., 2018) (Nakashima et al., 2020) (Rana et al., 2019) (Saito, 2010) (Tsuda et al., 2019) (Wang et al., 2009), have been proposed.

We hypothesize that a long-lasting inflammation of the decidua of CD is associated with HDP and preeclampsia. The present study examined the relationship of CD with HDP and preeclampsia and evaluated the effect of CD on the perinatal outcomes.

2. Methods

2.1. Ethics

This study was approved by the Ethics Committee of Shiga University of Medical Science (R2020-074). Information about the study was made public, and the opportunity for refusal was guaranteed as much as possible by an optout method, as suggested by the Ethics Committee.

2.2. Subject

The subjects were cases who delivered by cesarean section due to non-reassuring fetal status, fetal growth restriction, preterm delivery, fetal anomalies, and/or HDP between January 1, 2013 and June 30, 2020 and whose placentas were pathologically assessed. Cases at <22 weeks gestation, with premature rupture of the membranes, clinical chorioamnionitis, abruptio placenta and cases with abnormal morphological findings, such as placental tumor, were excluded from the study.

2.3. Immunohistochemistry

To diagnose CD, immunostaining of CD138 was performed to identify plasma cells of the decidua, as previously reported with slight modification (Kaku et al., 2020). In each case, the paraffin-embedded placental specimens containing the largest amount of decidua were used for the study. The specimens were cut into 4-μm-thick sections, placed

143 on a 42°C water bath, and mounted on 3-aminopropyltriethoxysaline-coated slides (FRC-
144 05; Matsunami, Osaka, Japan). Immunohistochemical staining reactions were performed
145 using the DISCOVERY XT IHC Research Platform (F. Hoffmann-La Roche, Ltd.,
146 Grenzacherstrasse, CH). Briefly, after deparaffinization and rehydration, the slides were
147 placed in Cell Conditioning 1 (F. Hoffmann-La Roche, Ltd., Grenzacherstrasse, CH) and
148 boiled at 98°C for 60 minutes. The slides were incubated with the monoclonal primary
149 antibodies for CD138 (B-A38; Nichirei Corp., Tokyo, Japan) for 32 minutes at room
150 temperature and incubated with the secondary antibody (Universal Secondary Antibody;
151 F. Hoffmann-La Roche, Ltd., Grenzacherstrasse, CH) for 12 minutes at room temperature,
152 followed by the development of DAB using the labeled streptavidin biotinylated antibody
153 reaction.
154
155 ***2.4.*** **Analyses**
156 The diagnosis of CD was performed by a blinded investigator. When one or more plasma
157 cells stained with CD138 were found in the decidua of 10 random high-power fields
158 (HPF), the patient was diagnosed with CD, as previously reported (Kaku et al., 2020)
159 (Khong et al., 2000). When findings of thrombosis, segmental avascular villi, and villous
160 stromal-vascular karyorrhexis were detected according to the Amsterdam Placental
161 workshop Group Consensus Statement (Khong et al., 2016), the diagnosis of fetal
162 vascular malperfusion (FVM) was made. After blinding, one pathologist assessed the
163 presence or absence of FVM, and then others analyzed the results.
164 The patients' characteristics, including age, gravidity, parity, body mass index (BMI),
165 achievement of pregnancy by *in vitro* fertilization (IVF pregnancy), gestational age at
166 delivery, birth weight, light for date infant status (LFD), Apgar scores at 1 and 5 minutes,

umbilical artery pH, presence of gestational diabetes mellitus (GDM) and HDP were extracted from the patients' records. When the HDP was present, the presence of severe HDP and type of HDP (preeclampsia, gestational hypertension and chronic hypertension) were extracted. When preeclampisa existed, the presence of early onset-type preeclampisa was ascertained.

Then, the patients were divided into two groups according to the presence (CD group) or absence (non-CD group) of CD. Each item was compared between the groups.

In addition, patients diagnosed with preeclampsia were divided into CD and non-CD groups and the parameters, including FVM, were compared between the groups.

Next, the patients were classified into those who developed preeclampsia (preeclampsia group) and those who did not develop any type of HDP (non-HDP group). Each parameter was compared between the preeclampsia and non-HDP groups.

We calculated the number of patients required for enrollment. We referred a report which showed that 32.1% of pregnant women with chronic endometritis (CE) developed preeclampsia when CE was not treated before pregnancy (Taranovska Ocapital O et al., 2020). HDP generally occurred at a rate of 5–10% (Hutcheon et al., 2011) (Li et al., 2021). However, this general population included patients with CE. CE has been reported to be observed in the uterine endometrium of 50–70% of women with a history of recurrent pregnancy loss (McQueen et al., 2015) (Zolghadri et al., 2011). Based on these references, we set the proportion of HDP unrelated to CE to 3.5%. Thus, we selected 0.05 for α, 0.8 for power β, 0.035 for P0 (the probability for a control patient), and 0.32 for P1 (the probabilityin an experimental subject). The calculation revealed that 21 experimental subjects and 53 control subjects were required. Alternatively, we referred to another report (Gundogan et al., 2010), which showed that the incidence rates of CD and HDP were

higher in an egg donation group in comparison to controls. CD was found in 42.4% (14/33) of the placentas in the egg donation group and 1.7% (2/60) of the placentas in the control group. Thus, we selected 0.017 for P0, and 0.424 for P1. The calculation resulted in sample sizes of 20 cases for the control group and 15 cases for the affected group.

The statistical analyses were performed using Graph Pad Prism 6 (GraphPad Software Inc., La Jolla, CA) and SPSS version 25 (SPSS Inc, Chicago, IL). Each dataset was analyzed for normal distribution using D'Agostino's *K*-squared test, and Student's *t*-test or the non-parametric Mann-Whitney *U*-test was used depending on the distribution pattern.

When the distribution pattern was judged as parametric, the result was shown as the mean ± SD. When the data were judged to show a non-parametric distribution, the results were shown as the median (interquartile range).

The statistical comparison of IVF pregnancy, LFD and HDP in the CD and non-CD group and IVF pregnancy, CD and LFD in the preeclmpsia and non-HDP group was performed using Fisher's exact test.

A stepwise logistic regression analysis of factors associated with preeclampsia or CD was performed to examine the independent effect of each of the following variables: age ≥40 years, BMI ≥25, multigravida, multiparity, IVF pregnancy, multiple pregnancy, preterm birth, CD, preeclampsia, LFD, Apgar score at 5 minutes ≤6, umbilical artery pH <7.1, and sex of the child. *P* values of <0.05 were considered to indicate statistical significance.

3. Results

3.1. Immunohistochemistry

Plasma cells infiltrating the decidua were identified by immunostaining for CD138 (Figure 1). Chorionic cells were stained with CD138 in all cases. When plasma cells were detected in the decidua, they often formed clusters.

3.2. Clinical parameters in the non-CD and CD groups

There were 54 patients in the non-CD group and 22 in the CD group. The patients' background clinical characteristics are shown in Table 1. There were no differences in age, BMI, gravidity, parity, or IVF pregnancy between the non-CD and CD groups. The rate of HDP was significantly higher in the CD group (P=0.002). Among the subtypes of HDP, only preeclampsia was found to have a significantly higher incidence in CD (P=0.0006). Gestational hypertension was found only in non-CD, although the difference in the incidence was not significant. Chronic hypertension was not found in either condition. The correlation between preeclampsia and CD was stronger than that between HDP and CD. The rate of severe HDP was significantly higher in the CD group (P=0.0008). There was no difference in the rate of GDM.Patients with CD gave birth at a significantly earlier gestational age (P=0.040), with a smaller birth weight (P=0.001), and with a higher rate of LFD (P=0.005). Furthermore, in the CD group, the Apgar score at 1 minute, Apgar score at 5 minutes, and umbilical cord arterial blood pH were lower (P=0.0003, 0.021 and 0.002).

Since gestational hypertension was only found in the non-CD group, chronic hypertension was not found in both groups and the correlation between preeclampsia and CD was stronger than that between HDP and CD, subsequent studies were limited to preeclampsia, with the preeclampsia group compared to the non-HDP group

3.3. Results of a stepwise logistic regression analysis with preeclampsia

A logistic regression analysis was performed with preeclampsia as the objective variable (Table 2). The explanatory variables were age ≥40 years, BMI ≥25, multigravida, multiparity, IVF pregnancy, multiple pregnancy, preterm birth, CD, LFD, Apgar score at 5 minutes ≤6, umbilical artery pH <7.1, and sex of the child. The following variables were found to be related to preeclampsia: age ≥40 years, BMI ≥25, multigravida, and CD. The results of the Hosmer and Lemeshow tests were P=0.957 and the discriminative predictive value was 81.7%.

3.4. Clinical parameters of the non-CD and CD groups with preeclampsia

In addition, a sub-analysis was performed to show the differences between patients with and without CD in the preeclmpsia group (Table 3). In this sub-analysis, there were no differences in age, gravidity, parity, BMI, or IVF pregnancy between the patients with and without CD. There was no significant differences between the two groups in the gestational age at delivery, the rate of preterm birth, the rate of LFD, or Apgar score at 5 minutes.

In this sub-analysis, the patients with CD were found to have a significantly lower birth weight (P=0.042). Furthermore, in this sub-analysis, the Apgar score at 1 minute tended to be lower, and the umbilical artery pH was significantly lower in patients with CD (P=0.034). CD was more frequently found in patients with early-onset type preeclampsia. The rate of FVM was not different.

3.5. Clinical parameters of the non- HDP and preeclampsia groups

The patients were classified into the non- HDP group (n=41) and the preeclampsia group

(n=31). The patients' background clinical characteristics are shown in Table 4. The preeclampsia group had significantly higher age and BMI values (P=0.047 and P=0.013, respectively) in comparison to the non- HDP group. Gravidity was significantly lower (P=0.031) in the preeclampsia group than in the non- HDP group and parity tended to be lower (P=0.073) in the preeclampsia group. The rate of IVF pregnancy tended to be higher in the preeclampsia group. There was no difference in the gestational age at delivery; however, the birth weight was lower (P=0.003) and the rate of LFD was higher (P=0.036) in the preeclampsia group. There were no differences in the Apgar scores at 1 and 5 minutes; however, the umbilical artery pH was lower (P=0.038) in the preeclampsia group.

CD was detected in 51.6% of the patients in the preeclampsia group and 17.1% of the patients in the non- HDP group (P=0.0024) (Table 4). The comparison of the number of CD138-positive cells in 10 random HPFs between the preeclampsia and non- HDP groups revealed that the number of CD138-positive cells was significantly higher in the preeclampsia group (P=0.0005) (Figure 2).

3.6. Results of a stepwise logistic regression analysis with CD

In the logistic regression analysis with CD as the objective variable (Table 2), the explanatory variables were age ≥40 years, BMI ≥25, multigravida, multiparity, IVF pregnancy, multiple pregnancy, preterm birth, preeclampsia, LFD, Apgar score at 5 minutes ≤6, umbilical artery pH <7.1, and sex of the child. The variables multiparity, preeclampsia, and LFD were found to be related to CD. The results of the Hosmer and Lemeshow tests were P=0.807, and the discriminative predictive value was 78.9%.

4. Discussion

In the present study, the incidence of HDP in the CD group was found to be higher than that in the non-CD group; preeclampsia was the only type of HDP for which th e incidence was significantly higher in the CD group. Furthermore, the incidence of CD in the preeclampsia group was higher than that in the non-HDP group. To the best of our knowledge, this is the first report to show an association between the presence of CD and the development of preeclampsia.

On the other hand, the present study also found that CD is a factor that worsens perinatal outcomes. In the past, CD was reported to be associated with fetal growth restriction (Bendon and Miller, 1990), intrauterine fetal death (Bendon and Miller, 1990) and preterm birth (Edmondson et al., 2009). Our data support these previous reports in terms of the higher rates of LFD and preterm birth.

CD is characterized by slight inflammation of the placental decidua. Regarding the relationship between inflammation and HDP, lipopolysaccharide has been reported to induce cytokine production and reduce EVT invasion (Anton et al., 2012). Moreover, numerous cytokines secreted by both trophoblast cells and decidua play a role in promoting and suppressing the infiltration of trophoblast cells during implantation (Sharma et al., 2016). We speculated that inflammation of the decidua might affect trophoblast invasion and spiral artery remodeling via the modulation of the immunity and the endometrial/decidual cell function (Di Pietro et al., 2013) (Kitazawa et al., 2021) (Matteo et al., 2009) (Pollheimer et al., 2018) (Tang et al., 2015) (Wu et al., 2017). Recently, we reported that patients in whom CD is diagnosed based on the examination a miscarriage specimen have a high rate of chronic endometritis (CE) (Kaku et al., 2020),

311 which involves slight inflammation of the endometrium (Kimura et al., 2019) (Kitaya et
312 al., 2016). Thus, a certain rate of CE before pregnancy peppepepersists after pregnancy
313 and becomes CD.
314 Moreover, patients in whom CE is detected before pregnancy have been reported to have
315 a higher incidence of miscarriage (Morimune et al., 2021) , preterm birth (Morimune et
316 al., 2021) and preeclampsia (Taranovska Ocapital O et al., 2020). Taken together, we
317 speculated that endometrial inflammation may persist in the early-stage decidua in certain
318 cases and that persistent inflammation might inhibit spiral artery remodeling, resulting in
319 the development of preeclampsia.
320 On the other hand, it is possible that abnormal immune tolerance between the motherand
321 infant caused inflammation and CD. The egg donor IVF placenta, in which the mother
322 and embryo are completely immunogenetically unrelated, has been reported to have a
323 significantly higher incidence of CD than the non-donor IVF placenta (Gundogan et al.,
324 2010). These differences were suggested to result from differentially modulated immune
325 activity at the maternal-fetal interface of egg donor pregnancies (Gundogan et al., 2010,
326 Saito et al., 2016). Preterm births are reported to be more common in egg donation
327 pregnancies, suggesting that CD may be associated with preterm birth (Gundogan et al.,
328 2010). Previous studies have demonstrated that egg donor pregnancies are associated with
329 an increased risk of preeclampsia (Blazquez et al., 2016) (Masoudian et al., 2016).
330 Abnormal immune tolerance between mothers and infants is strongly supported as a cause
331 of preeclampsia. We speculated that a host versus graft rejection phenomenon or an effort
332 to suppress rejection causes CD, and that these immunological abnormalities also cause
333 preeclampsia (Morita et al., 2020) (Redman and Sargent, 2010) (Tsuda et al., 2018).
334 It is now clear that bacterial flora is present in many organs of adult humans. The

predominant idea at present is that the bacterial flora is present in the placenta, although some reports have denied such a thing. However, the presence of bacterial flora in the endometrium, regardless of the presence of bacteria in the placenta, has been confirmed not only via next-generation sequencing (Chen et al., 2017) but also in simple culture studies (Benner et al., 2018) (Cowling et al., 1992) (Moller et al., 1995). Given these results, we believe that plasma cells in the decidua could develop due to antigens in the maternal endometrium or its decidualized endometrium although it is possible that they develop due to certain placental antigens which derived from the fetus or antigens existing in the placenta such as bacteria.

The strength of this study is that it is the first report to clearly reveal the association between preeclampsia and CD. However, the present study is associated with some limitations. This was a retrospective study and subjects were only selected when the placenta was assessed, after the extraction of cases involving delivery by cesarean section due to non-reassuring fetal status, fetal growth restriction, preterm delivery, fetal anomaly, and/or HDP. Thus, although we confirmed the results by a logistic regression analysis, there was a selection bias.

In the future, it is expected that preeclampsia might be fundamentally treated by elucidating the pathophysiology of CD. In particular, in a certain number of cases, CD was derived from CE. In cases involving CE, the live birth rate has been reported to be increased by antibiotic treatment before pregnancy (Cicinelli et al., 2015) (Kitaya et al., 2017). In the future study, it would be worthwhile evaluating whether the curative treatment of CE before pregnancy can prevent the onset of preeclampsia.

In conclusion, based on the retrospective examination of placenta, we found that patients with CD had a significantly higher incidence of preeclampsia and CD is considered to be a factor that is associated with poor perinatal outcomes.

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Declaration of Competing Interest

None of the authors has any conflict of interest related to this manuscript.

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Figure Legends

Figure 1. Immunohistochemistry of CD138 for placenta.

a. b. Plasma cells in the decidua immunostained by CD138 are detected in chronic deciduitis.

c. d. Plasma cells in the decidua are not detected in non-chronic deciduitis.

a. c. Bar = 500 μm

b. d. Bar = 100 μm

Figure 2. The number of CD138-positive cells in 10 HPFs.

The number of CD138-positive cells in 10 random HPFs was significantly higher in the preeclampsia group than in the non- HDP group.

There was a case with a markedly high number of CD138-positive cells. Five sections from different placental parts were pathologically examined to confirm the result (Supplemental figure 1) . As results, over 100 CD138-positive cells in 10 random HPFs were found to have infiltrated into the decidua in all specimens. This was a case of preeclampsia with delivery at 32 weeks' gestation in which the fetal heart rate pattern rapidly deteriorated. Among all cases examined in the present study, this was the only one for whom category-1 emergency caesarean section(Lucas et al., 2000) was performed in the preterm period. The infant was LFD, and the Apgar scores at 1 and 5 minutes (1 point, 5 points) and umbilical arterial blood pH (6.882) were extremely low. This result might therefore indicate the serious effects of CD138-positive cells in the decidua on the pathophysiology of HDP and/or the prognosis of the affected fetus.

Supplemental figure 1. Immunohistochemistry of CD138 for the placenta of the case

586 **with markedly high numbers of CD138-positive cells.**

587 Over 100 CD138-positive cells in 10 random HPFs were found to have infiltrated into the

588 decidua of the placenta preserved in paraffin-embedded specimens.

589 a. b. c. d. e. Bar = 500 μm

590 f. Bar = 100 μm

Table 1. Characteristics and delivery outcomes in the non-CD and CD groups

	non-CD N=54	CD N=22	P value
Age (years)	33.98±5.11	33.82±5.73	NS
Gravity, median (IQR)	2.00 (1.00-2.00)	1.50 (1.00-2.00)	NS
Parity, median (IQR)	0 (0-1.00)	0 (0-1.00)	NS
BMI (kg/m^2)	22.19±3.88	22.05±3.66	NS
IVF pregnancy	31.5% (17/54)	27.2% (6/22)	NS
HDP	35.2% (19/54)	72.7% (16/22)	<.01
Preeclampsia	27.8% (15/54)	72.7% (16/22)	<.001
Gestational hypertension	7.4% (4/54)	0% (0/22)	NS
Chronic hypertension	0% (0/54)	0% (0/22)	NS
Severe HDP	29.6% (16/54)	72.7% (16/22)	<.001
GDM	9.2% (5/54)	9.0% (2/22)	NS
Gestational age at delivery	35.30±2.57	33.73±3.67	<.05
Birth weight (g)	2270±645.28	1752±596.24	0.001
LFD	26.9% (18/67)	60.9% (14/23)	<.01
Apgar score at 1 minute	7.48 ±1.19	5.96 ±2.56	<.001
Apgar score at 5 minutes, median (IQR)	9.00 (9.00-9.00)	9.00 (8.00-9.00)	<.03
Umbilical artery pH, median (IQR)	7.313 (7.281-7.343)	7.281 (7.206-7.301)	<.01

BMI, Body mass index; CD, Chronic deciduitis; GDM, Gestational diabetes mellitus; HDP, Hypertensive disorders of pregnancy; IVF, *In vitro* fertilization; LFD, Light-for-date infant; NS, Not significant

Table 2. Logistic regression analysis of factors associated with preeclampsia and CD

	Variable	Odds ratio	95% CI	P value
Preeclampsia	Age ≥40 years	57.3	3.7-877.7	<.01
	BMI ≥25	16.36	1.8-147.5	<.03
	Multigravida	0.08	0.01-0.4	<.01
	CD	12.1	1.9-73.7	<.01
CD	Multiparity	4.9	1.1-20.8	<.03
	Preeclampsia	7.7	1.9-30.2	<.01
	LFD	5.9	1.6-21.3	<.01

BMI, Body mass index; CD, Chronic deciduitis; CI, Confidence interval; LFD, Light-for-date infant.

Table 3. Characteristics and outcomes of the preeclampsia patients in the non-CD and CD groups .

	non-CD N=15	CD N=16	P value
Age (y)	36.80±4.32	34.25±6.46	NS
Gravity	1.53±0.63	1.81±1.33	NS
Parity, median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	NS
BMI (kg/m^2)	24.94±5.30	22.37±4.04	NS
IVF pregnancy	40.0% (6/15)	37.5% (6/16)	NS
Gestational age at delivery	35.07±3.32	33.13±4.06	NS
Preterm birth	53.3% (8/15)	81.2% (13/16)	NS
Birth weight (g)	2116±816.70	1577±562.23	<.05
LFD	40.0% (6/15)	62.5% (10/16)	NS
Apgar score at 1 minute	7.53±0.91	6.18±2.65	<.1
Apgar score at 5 minutes, median (IQR)	9.00 (9.00-9.00)	9.00 (8.25-9.00)	NS
Umbilical artery pH	7.306±0.04	7.228±0.13	<.05
Early-onset type PE	40.0% (6/15)	75.0% (12/16)	<.1
FVM	60.0% (9/15)	87.5% (14/16)	NS

BMI, Body mass index; CD, Chronic deciduitis; FVM, Fetal vascular malperfusion; IVF, *In vitro* fertilization; LFD, Light-for-date infant; NS, Not significant.

Table 4. Characteristics and delivery outcomes of the non-HDP and preeclampsia groups

	non- HDP N=41	preeclampsia N=31	P value
Age (y)	32.8±4.91	35.4±5.65	<.05
Gravidity	2.34±1.37	1.67±1.07	<.05
Parity, median (IQR)	0.0 (0.0-1.0)	0.0 (0.0-1.0)	<.1
BMI (kg/m^2)	21.34 ±2.56	23.61±4.85	<.03
IVF pregnancy	26.8% (11/41)	38.7% (12/31)	<.1
Gestational age at delivery	35.34±2.17	34.06±3.86	NS
Birth weight (g)	2280±575.56	1838±745.10	<.01
LFD	27.8% (15/54)	51.6% (16/31)	<.05
Apgar score at 1 minute, median (IQR)	8.00 (6.00-8.00)	8.00 (7.00-8.00)	NS
Apgar score at 5 minutes, median (IQR)	9.00 (8.00-9.00)	9.00 (8.00-9.00)	NS
Umbilical artery pH, median (IQR)	7.316 (7.289-7.343)	7.293 (7.258-7.325)	<.05
CD	17.1% (7/41)	51.6% (16/31)	<.01

BMI, Body mass index; CD, Chronic deciduitis; HDP, Hypertensive disorders of pregnancy; IVF, *In vitro* fertilization; LFD, Light-for-date infant; NS, Not significant.