

Mild thrombocytopenia indicating maternal organ damage in pre-eclampsia: a cross-sectional study

Michinori Mayama (✉ m_mayama@protonmail.com)

Hokkaido University Hospital <https://orcid.org/0000-0001-6630-9869>

Mamoru Morikawa

Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine

Takashi Yamada

Department of Obstetrics and Gynecology, Japan Community Health Care Organization Hokkaido Hospital

Takeshi Umazume

Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine

Kiwamu Noshiro

Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine

Kinuko Nakagawa

Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine

Yoshihiro Saito

Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine

Kentaro Chiba

Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine

Satoshi Kawaguchi

Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine

Hidemichi Watari

Department of Obstetrics and Gynecology, Hokkaido University Graduate School of Medicine

Research article

Keywords: Cut-off value, Maternal organ damage, Pre-eclampsia, Preterm delivery, Thrombocytopenia

Posted Date: November 12th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-103716/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published on January 28th, 2021. See the published version at <https://doi.org/10.1186/s12884-021-03564-4>.

Abstract

Background

Currently, there is a disagreement between guidelines regarding platelet count cut-off values as a sign of maternal organ damage in pre-eclampsia; the American College of Obstetricians and Gynecologists guidelines state a cut-off value of $<100 \times 10^9/L$; however, the International Society for the Study of Hypertension in Pregnancy guidelines specify a cut-off of $<150 \times 10^9/L$. We evaluated the effect of mild thrombocytopenia: platelet count $<150 \times 10^9/L$ and $\geq 100 \times 10^9/L$ on clinical features of pre-eclampsia to examine whether mild thrombocytopenia reflects maternal organ damage in pre-eclampsia.

Methods

A total of 264 women were enrolled in this study. Participants were divided into three groups based on platelet count levels at delivery: normal, $\geq 150 \times 10^9/L$; mild thrombocytopenia, $<150 \times 10^9/L$ and $\geq 100 \times 10^9/L$; and severe thrombocytopenia, $<100 \times 10^9/L$. Risk of severe hypertension, utero-placental dysfunction, maternal organ damage, preterm delivery, and neonatal intensive care unit admission were analyzed based on platelet count levels. Adjusted relative risk were calculated with a Poisson regression analysis with a robust error.

Results

Platelet counts indicated normal levels in 189 patients, mild thrombocytopenia in 51 patients, and severe thrombocytopenia in 24 patients. The adjusted risk ratios of severe thrombocytopenia were 2.11 [95% confidence interval, 1.61–2.77] for maternal organ damage except thrombocytopenia, 1.24 [1.01–1.53] for preterm delivery <34 gestational weeks, and 1.16 [1.02–1.32] for neonatal intensive care unit admission. On the other hand, the adjusted risk ratios of mild thrombocytopenia were 1.06 [0.86–1.30] for severe hypertension, 1.17 [0.74–1.83] for utero-placental dysfunction, 0.96 [0.41–2.24] for maternal organ damage except thrombocytopenia, 0.89 [0.60–1.31] for preterm delivery <34 gestational weeks, and 0.96 [0.75–1.23] for neonatal intensive care unit admission.

Conclusions

Mild thrombocytopenia was not related with severe features of pre-eclampsia and would not be suitable as a sign of maternal organ damage.

1. Background

Hypertensive disorders of pregnancy (HDP) can cause hypertension and maternal organ damage due to endothelial dysfunction [1,2]. Among patients with HDP, women who develop maternal organ damage in addition to hypertension are diagnosed with pre-eclampsia, even if they do not develop proteinuria. Coagulation disorders are considered a sign of maternal organ damage in preeclamptic patients [1, 2].

Thrombocytopenia is the most frequently detected coagulation disorder in pre-eclampsia and likely occurs as a result of the injured endothelium activating platelets, leading to elevated consumption of platelets [3, 4]. Pre-eclampsia is the most common cause of thrombocytopenia with evidence of thrombotic microangiopathy in the second and third trimester of pregnancy [5].

Severe thrombocytopenia: platelet count (PC) $<100 \times 10^9/L$ is a sign of severe pre-eclampsia, and termination of pregnancy should be considered [1]. However, the clinical significance of mild thrombocytopenia ($\geq 100 \times 10^9/L$ and $<150 \times 10^9/L$) in pre-eclampsia remains controversial. The International Society for the Study of Hypertension in Pregnancy guidelines state PC levels $<150 \times 10^9/L$ as a sign of maternal organ damage, whereas the American College of Obstetricians and Gynecologists guidelines state a cut-off value of $<100 \times 10^9/L$ [1, 2]. Although termination of pregnancy must be considered in the context of gestational age and other clinical and laboratory results in combination with PC levels, the classification of HDP is affected by whether mild thrombocytopenia is included as a sign of maternal organ damage. Therefore, the discrepancy in PC cut-off values between the two major guidelines make it difficult to compare studies based on these different guidelines. Actually, a sign of maternal organ damage was included in the criteria of classification of HDP in May 2018 in Japan and it increased the number of women who were diagnosed with pre-eclampsia [6]. To assess whether mild thrombocytopenia reflects maternal organ damage in patients with pre-eclampsia, we examined the impact of mild thrombocytopenia on severity of pre-eclampsia and perinatal outcomes.

2. Methods

2.1 Study Population

Women diagnosed with HDP and who delivered at Hokkaido University Hospital and Japan Community Health Care Organization Hokkaido Hospital between April 2010 and May 2019 were eligible for this study. Women who were <18 years old at delivery or transferred to other hospitals before delivery were excluded. Furthermore, women were excluded if their thrombocytopenia was not related to HDP, baby had severe congenital anomaly, twin pregnancy, and data were insufficient. Among the patients with HDP, women who were diagnosed with gestational hypertension and chronic hypertension were also excluded.

2.2 Data Collection

Diagnosis and classification of HDP were conducted based on the International Society for the Study of Hypertension in Pregnancy and Japan Society for the Study of Hypertension in Pregnancy guidelines [2, 7]. Participants were divided into three groups according to PC levels at delivery: normal, $PC > 150 \times 10^9/L$; mild thrombocytopenia, $\geq 100 \times 10^9/L$ and $<150 \times 10^9/L$; and severe thrombocytopenia, $<100 \times 10^9/L$. We analyzed the incidence of severe hypertension (systolic blood pressure >160 mmHg or diastolic blood pressure >110 mmHg), maternal organ damage, utero-placental dysfunction, and gestational age at onset of pre-eclampsia, as well as the rate of neonatal intensive care unit (NICU) admission and preterm delivery <34 gestational weeks (GW). Maternal organ damage and utero-placental

dysfunction were defined based on the guidelines of the International Society for the Study of Hypertension in Pregnancy guidelines, as shown in Table 1 [2].

2.3 Statistical Analyses

Statistical analyses were conducted using Stata/SE version 15.1 (StataCorp). The normality of the data was analyzed by histogram in terms of skewness and kurtosis. Continuous data are reported as mean \pm standard deviation. Categorical variables are expressed as frequency and percentage. Statistical significance was calculated using independent t-test for continuous data and chi-square test for categorical variables. Logistic regression analysis is often used to calculate adjusted odds ratio, which approximates the adjusted relative risk when the outcome incidence is low. However, odds ratio overestimates relative risk for more common outcomes (>10 %) [8]. Therefore, to calculate the relative risk (RR) and 95% confidence interval (CI), we used a Poisson regression analysis with a robust error variance. Maternal age and PC levels were included as covariates to assess the RR for severe hypertensin, utero-placental dysfunction, and maternal organ damage except thrombocytopenia. In addition to maternal age and PC levels, we included severe hypertension, utero-placental dysfunction, and maternal organ damage except thrombocytopenia as covariates to assess the RR for preterm delivery <34 GW and NICU admission.

2.4 Ethical Approval

This study was approved by the institutional review board of Hokkaido University Hospital (019-0070) and Japan Community Health Care Organization Hokkaido Hospital (2020-4). The committees did not require informed consent for this retrospective study. We put information of this study on Hokkaido University's and Japan Community Health Care Organization Hokkaido Hospital's home page with the opportunity to opt out.

3. Results

There were 436 women who were diagnosed with HDP during the study period, and 172 of them fulfilled the exclusion criteria and were not included in the analysis. Therefore, 264 women were evaluated in this study (Fig. 1). PC levels were normal in 189 patients, 51 had mild thrombocytopenia, and 24 had severe thrombocytopenia. Table 2 shows the clinical characteristics based on PC levels. The clinical characteristics were not different between patients with normal platelet count and those with mild thrombocytopenia. Table 3 presents the perinatal outcomes and clinical features of pre-eclampsia based on PC levels. GW at the onset of pre-eclampsia and the day of delivery were similar between patients with normal PC and those with mild thrombocytopenia. The incidence of preterm delivery <34 GW (normal PC: 34.9%, mild thrombocytopenia: 35.3%, $p = 0.960$), NICU admission (normal PC: 53.4%, mild thrombocytopenia: 56.9%, $p = 0.663$), severe hypertension (normal PC: 66.7%, mild thrombocytopenia: 70.6%, $p = 0.596$), utero-placental dysfunction (normal PC: 28.6%, mild thrombocytopenia: 33.3%, $p = 0.249$), and maternal organ damage except thrombocytopenia (normal PC: 12.2%, mild thrombocytopenia: 11.8%, $p = 0.937$) were also equivalent between the two group.

Table 4 shows the age adjusted RRs of mild thrombocytopenia for severe hypertension (RR:1.06, 95% CI: 0.86–1.30), utero-placental dysfunction (RR: 1.17, 95% CI: 0.74–1.83), and maternal organ damage except thrombocytopenia (RR: 0.96, 95% CI: 0.41–2.24). Table 5 represents the adjusted RRs of mild thrombocytopenia for preterm delivery <34 GW and NICU admission. While severe hypertension, utero-placental dysfunction, and maternal organ damage except thrombocytopenia increased the risk of preterm delivery and NICU admission, mild thrombocytopenia was not a risk factor of preterm delivery <34 GW (RR: 0.89, 95% CI: 0.60–1.31) and NICU admission (RR: 0.96, 95% CI: 0.75–1.23).

Clinical characteristics, perinatal outcomes, and clinical features of pre-eclampsia in patients with severe thrombocytopenia are shown in additional file 1 and 2. The clinical characteristics were similar between patients with normal platelet count and those with severe thrombocytopenia. Although the incidence of severe hypertension and utero-placental dysfunction was not different between the patients with normal platelet count and those with severe thrombocytopenia, the incidence of maternal organ damage, except for thrombocytopenia, was higher in patients with severe thrombocytopenia (normal PC: 12.2%, severe thrombocytopenia: 54.2%, $p < 0.001$). In patients with severe thrombocytopenia, the GW at the onset of pre-eclampsia was earlier (normal PC: 34.1 ± 4.4 , severe thrombocytopenia: 29.7 ± 5.5 , $p < 0.001$), and the rates of preterm delivery <34GW (normal PC: 34.9%, severe thrombocytopenia: 66.7%, $p = 0.003$) and NICU admission (normal PC: 53.4%, severe thrombocytopenia: 87.5%, $p = 0.001$) were higher in patients with severe thrombocytopenia. Additional file 3 and 4 present the adjusted RRs of severe thrombocytopenia. Severe thrombocytopenia was found to be a significant risk factor of maternal organ damage, except for thrombocytopenia, (RR: 2.11, 95% CI: 1.61–2.77); preterm delivery <34GW (RR: 1.24, 95% CI: 1.01–1.53); and NICU admission (RR: 1.16, 95% CI: 1.02–1.32).

4. Discussion

The results of the present study revealed that mild thrombocytopenia ($\geq 100 \times 10^9/L$ and $< 150 \times 10^9/L$) is not a risk factor for developing severe features of pre-eclampsia, including severe hypertension, maternal organ damage, and utero-placental dysfunction. Although physicians decide the timing of delivery in patients with pre-eclampsia based on GW and various clinical aspects in addition to PC counts, the rates of preterm delivery and NICU admission may be affected by the levels of PC counts, because thrombocytopenia is included as a sign of maternal organ damage. However, preterm delivery and NICU admission rates in patients with mild thrombocytopenia were not different from the rates in patients with normal PC. On the other hand, severe thrombocytopenia was a risk factor of developing a maternal organ damage, except for thrombocytopenia. Although the rates of preterm delivery and NICU admission were higher in patients with severe thrombocytopenia than in patients with normal PC, the results might have been biased because severe thrombocytopenia is an indicator of pregnancy termination [1]. However, the onset of pre-eclampsia, which is not biased by PC levels, was earlier in patients with severe thrombocytopenia than in patients with normal PC. Early onset of pre-eclampsia is associated with worse outcomes in both mother and baby [9]. These findings support that PC levels $\geq 100 \times 10^9/L$ and $< 150 \times 10^9/L$ does not reflect a sign of maternal organ damage in pre-eclampsia.

Gestational thrombocytopenia (GT) is defined as PC levels $<150 \times 10^9/L$, with the exclusion of other possible diagnoses [5]. GT occurs in 4.4% to 11.6% of pregnancies and accounts for almost 75% of thrombocytopenia in pregnancy [10–12]. Since there are no available biomarkers to provide a definite diagnosis of GT, some cases of thrombocytopenia detected in HDP patients may not reflect the disease progression and may be a result of GT. In addition, only 1% to 5% women with GT develop PC levels $<100 \times 10^9/L$, and GT does not usually affect perinatal outcomes [5]. Therefore, this could explain why mild thrombocytopenia was not related with worse perinatal outcomes in our study, as thrombocytopenia was not caused by pre-eclampsia.

Blood coagulation disorders, including thrombocytopenia, are a sign of maternal organ damage; therefore, patients with thrombocytopenia are considered as severe pre-eclampsia even with blood pressure levels $<160/110$ mmHg and no other signs of maternal organ damage [1, 2]. If the majority of cases of mild thrombocytopenia are not associated with worse maternal and neonatal outcomes, using PC levels $<150 \times 10^9/L$ as a cut-off value of a sign of maternal organ damage may increase unnecessary hospitalization and iatrogenic preterm delivery, particularly after 34 GW.

Pre-eclampsia is a progressive disease and PC levels may decrease as the disease progresses. Our findings indicate that mild thrombocytopenia is not a severe feature of pre-eclampsia; however, PC levels may decrease in patients with mild thrombocytopenia as pre-eclampsia progresses and become severe thrombocytopenia. Evaluation of the speed of PC decrease and the rate of PC decrease from the baseline will give further information to predict the deterioration of pre-eclampsia. Previous studies have reported that platelet indices, such as mean platelet volume and platelet distribution width, were associated with pre-eclampsia development and severity [13–15]. Analysis of platelet indices in addition to PC may help identify patients with mild thrombocytopenia in which PC levels will progressively decrease.

In Japan, thrombocytopenia was not included in the criteria of diagnosis and severity of pre-eclampsia until May 2018. The protocol for HDP patient management in Hokkaido University Hospital and Japan Community Health Care Organization Hokkaido Hospital was not changed after the Japanese criteria revision. Therefore, clinicians' decisions would not have been affected the discrepancy in PC cut-off value in the present study.

This study has several limitations. This was a retrospective study; therefore, the timing of termination was decided based on the clinical decisions of the doctors in each hospital. Although serum biomarkers, such as the ratio of soluble fms-like tyrosine kinase to placental growth factor, are associated with development of pre-eclampsia [16], they were not widely available in Japan during the study period. Thus, we were unable to examine the association between mild thrombocytopenia and those biomarkers. Finally, low-dose aspirin is useful for prevention of pre-eclampsia in high-risk patients [17]. However, the rate of low-dose aspirin usage was very low in our study. Therefore, it is difficult to determine whether our findings are adaptable for patients using low-dose aspirin.

5. Conclusion

Despite these limitations, this study implies that mild thrombocytopenia in pre-eclampsia is not related with severe features of pre-eclampsia, and would not be suitable as a sign of maternal organ damage in patients with pre-eclampsia. PC levels $<100 \times 10^9/L$ may be better cut-off value as a sign of maternal organ damage in pre-eclampsia.

Abbreviations

CI: confidence interval

GT: gestational thrombocytopenia

GW: gestational weeks

HDP: hypertensive disorders of pregnancy

NICU: neonatal intensive care unit

RR: relative risk

PC: platelet count

Declarations

Ethics approval and consent to participate

This study was approved by the institutional review board of Hokkaido University Hospital (019-0070) and Japan Community Health Care Organization Hokkaido Hospital (2020-4). The committees did not require informed consent for this retrospective study. We put information of this study on Hokkaido University's and Japan Community Health Care Organization Hokkaido Hospital's home page with the opportunity to opt out.

Consent for publication

Not required

Availability of data and materials

The datasets used and/or analysed during the current study will be available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author's contribution

All listed authors meet criteria for authorship. MM made substantial contributions to conceptualization, design of the work, and drafting the work. MM made substantial contributions to conceptualization, the acquisition, and the analysis. TY and TU made substantial contributions to interpretation of data. KN and KN made substantial contributions to the acquisition, and the analysis. YS and KC made substantial contributions to design of work. SK and HW made substantial contributions to drafting and revising work. All authors approved the submitted version, and agreed to be personally accountable for their contributions to the work.

Acknowledgements

The authors would like to thank Enago (<https://www.enago.jp>) for the English language review.

References

1. Khodzhaeva ZS, Kogan YA, Shmakov RG, Klimenchenko NI, Akatyeva AS, Vavina OV, et al. Clinical and pathogenetic features of early- and late-onset pre-eclampsia. *J Matern Fetal Neonatal Med.* 2016; 29: 2980-6.
2. McNutt LA, Wu C, Xue X, Hafner JP. Estimating the relative risk in cohort studies and clinical trials of common outcomes. *Am J Epidemiol.* 2003; 157: 940-3.
3. Makino S, Takeda J, Takeda S, Watanabe K, Matsubara K, Nakamoto O, et al. New definition and classification of "Hypertensive Disorders of Pregnancy (HDP)". *Hypertens Res Pregnancy.* 2019; 7: 1-5.
4. Mayama M, Morikawa M, Umazume T, Nakagawa K, Hosokawa A, Yamaguchi M, et al. Increase in the number of patients diagnosed using the new classification of hypertensive disorders of pregnancy in Japan. *J Obstet Gynaecol Res.* 2019; 45: 1118-26.
5. Cines DB, Levine LD. Thrombocytopenia in pregnancy. *Blood.* 2017; 130: 2271-7.
6. Thalor N, Singh K, Pujani M, Chauhan V, Agarwal C, Ahuja R. A correlation between platelet indices and pre-eclampsia. *Hematol Transfus Cell Ther.* 2019; 41: 129-33.
7. Juan P, Stefano G, Antonella S, Albana C. Platelets in pregnancy. *J Prenat Med.* 2011; 5: 90-2.
8. Brown MA, Magee LA, Kenny LC, Karumanchi SA, McCarthy FP, Saito S, et al. Hypertensive Disorders of Pregnancy: ISSHP Classification, Diagnosis, and Management Recommendations for International Practice. 2018; 72: 24-43.
9. American College of Obstetricians and Gynecologists; Task Force on Hypertension in Pregnancy. Hypertension in pregnancy. Report of the American College of Obstetricians and Gynecologists' Task Force on Hypertension in Pregnancy. *Obstet Gynecol.* 2013; 122: 1122-31.

10. Practice bulletin no. 166: thrombocytopenia in pregnancy. *Obstet Gynecol.* 2016; 128: e43-e53.
11. Burrows RF, Kelton JG. Thrombocytopenia at delivery: A prospective survey of 6715 deliveries. *Am J Obstet Gynecol.* 1990; 162: 731-4.
12. Gernsheimer T, James AH, Stasi R. How I treat thrombocytopenia in pregnancy. *Blood.* 2013; 121: 38-47.
13. Freitas LG, Alpoim PN, Komatsuzaki F, Carvalho Md, Dusse LM. Pre-eclampsia: are platelet count and indices useful for its prognostic? 2013; 18: 360-4.
14. Yang SW, Cho SH, Kwon HS, Sohn IS, Hwang HS. Significance of the platelet distribution width as a severity marker for the development of pre-eclampsia. *Eur J Obstet Gynecol Reprod Biol.* 2014; 175: 107-11.
15. AlSheeha MA, Alaboudi RS, Alghasham MA, Iqbal J, Adam I. Platelet count and platelet indices in women with pre-eclampsia. *Vasc Health Risk Manag.* 2016; 12: 477-80.
16. Zeisler H, Llurba E, Chantraine F, Vatish M, Staff AC, Sennström M, et al. Predictive Value of the sFlt-1:PIGF Ratio in Women with Suspected Pre-eclampsia. *N Engl J Med.* 2016; 374: 13-22.
17. Rolnik DL, Wright D, Poon LC, O'Gorman N, Syngelaki A, de Paco Matallana C, et al. Aspirin versus placebo in pregnancies at high risk for preterm pre-eclampsia. *N Engl J Med.* 2017; 377: 613-22.

Tables

Table 1 The criteria of maternal organ damage and utero-placental dysfunction

I Liver involvement without underlying disease AST or ALT >40 IU/L with or without right upper quadrant or epigastric abdominal pain
I Acute kidney injury Serum creatine level ≥ 90 $\mu\text{mol/L}$; 1.0 mg/dL
I Neurological complications Eclampsia, altered mental status, blindness, stroke, clonus, severe headache, or persistent visual scotoma
I Blood coagulation disorders Thrombocytopenia: platelet count $< 150 \times 10^9/\text{L}$, disseminated intravascular coagulation, or hemolysis
I Uteroplacental dysfunction Fetal growth restriction [*] , abnormal umbilical artery doppler waveform [†] , or stillbirth [‡]

*: Estimated fetal weight < -1.5 standard deviation without chromosomal abnormality and multiple congenital anomaly syndrome

†: Absent or reversal of end diastolic flow, or extremely high pulsatility index or resistance index

‡: The cases of stillbirth with chromosomal abnormality or multiple congenital anomaly syndrome are excluded

AST, aspartate transaminase; ALT, alanine transaminase

Table 2 Clinical characteristics in patients with normal platelet count level and mild thrombocytopenia

	Normal (n = 189)	Mild thrombocytopenia (n = 51)	P value
Maternal Age (y.o) [*]	33.9 ± 5.2	34.5 ± 5.1	0.475
Primipara [†]	115 (61.2)	33 (64.7)	0.645
Previous history of pre-eclampsia [†]	19 (10.1)	3 (5.9)	0.360
Low-dose aspirin for prevention [†]	2 (1.1)	2 (3.9)	0.156
Cesarean delivery [†]	146 (77.3)	41 (82.0)	0.469

*: mean ± standard deviation, statistical significance was calculated with independent t-test

†: n (%), statistical significance was calculated with chi-square test

Normal: platelet count $>150 \times 10^9/L$, Mild thrombocytopenia: platelet count $< 150 \times 10^9/L$ and $\geq 100 \times 10^9/L$

Table 3 Pre-eclampsia outcomes and clinical features in patients with normal platelet count level and mild thrombocytopenia

	Normal (n = 189)	Mild thrombocytopenia (n = 51)	P value
GW at the onset of pre-eclampsia (weeks) *	34.1 ± 4.4	33.7 ± 3.8	0.578
GW at the day of delivery (weeks) *	35.1 ± 3.9	34.9 ± 3.6	0.652
Preterm delivery <34 GW [†]	66 (34.9)	18 (35.3)	0.960
NICU admission [†]	101 (53.4)	29 (56.9)	0.663
Severe hypertension [†]	126 (66.7)	36 (70.6)	0.596
Utero-placental dysfunction [†]	54 (28.6)	17 (33.3)	0.249
Maternal organ damage except thrombocytopenia [†]	23 (12.2)	6 (11.8)	0.937

*: mean ± standard deviation, statistical significance was calculated with independent t-test

†: n (%), statistical significance was calculated with chi-square test

Normal: platelet count $>150 \times 10^9/L$, Mild thrombocytopenia: platelet count $< 150 \times 10^9/L$ and $\geq 100 \times 10^9/L$

GW, gestational weeks; NICU, neonatal intensive care unit

Table 4 Relative mild thrombocytopenia risk for severe hypertension, utero-placental dysfunction, and maternal organ damage except thrombocytopenia.

	RR	95% CI	p value
Severe hypertension			
Age*	1.00	0.92–1.09	1.000
Mild thrombocytopenia	1.06	0.86–1.30	0.585
Utero-placental dysfunction			
Age*	1.01	0.84–1.21	0.924
Mild thrombocytopenia	1.17	0.74–1.83	0.505
Maternal organ damage except thrombocytopenia			
Age*	1.09	0.81–1.45	0.569
Mild thrombocytopenia	0.96	0.41–2.24	0.920

*: Relative risk of 5 years increase in age

Mild thrombocytopenia: platelet count $< 150 \times 10^9/L$ and $\geq 100 \times 10^9/L$

RR, relative risk; CI, confidence interval

Table 5 Relative risk of mild thrombocytopenia for preterm delivery and NICU admission.

	RR	95% CI	p value
Preterm delivery <34 GW			
Age*	1.05	0.89–1.24	0.536
Mild thrombocytopenia	0.89	0.60–1.31	0.551
Severe hypertension	1.56	1.03–2.36	0.035
utero-placental dysfunction	2.48	1.79–3.42	<0.001
maternal organ damage except thrombocytopenia	1.42	0.95–2.13	0.087
NICU admission			
Age*	1.07	0.97–1.18	0.184
Mild thrombocytopenia	0.96	0.75–1.23	0.769
Severe hypertension	1.16	0.91–1.48	0.217
utero-placental dysfunction	2.43	1.99–2.98	<0.001
maternal organ damage except thrombocytopenia	1.56	1.22–1.98	<0.001

Mild thrombocytopenia: platelet count $< 150 \times 10^9/L$ and $\geq 100 \times 10^9/L$

RR, relative risk; CI, confidence interval; GW, gestational weeks; NICU, neonatal intensive care unit

Supplementary Information

Supplementary information accompanies this paper.

Additional file 1. Clinical characteristics in patients with normal platelet count and severe thrombocytopenia. Additional file 2. Pre-eclampsia outcomes and clinical features in patients with normal platelet count level and severe thrombocytopenia

. Additional file 3. Relative severe thrombocytopenia risk for severe hypertension, utero-placental dysfunction, and maternal organ damage except thrombocytopenia. Additional file 4. Relative risk of severe thrombocytopenia for preterm delivery and NICU admission.

Figures

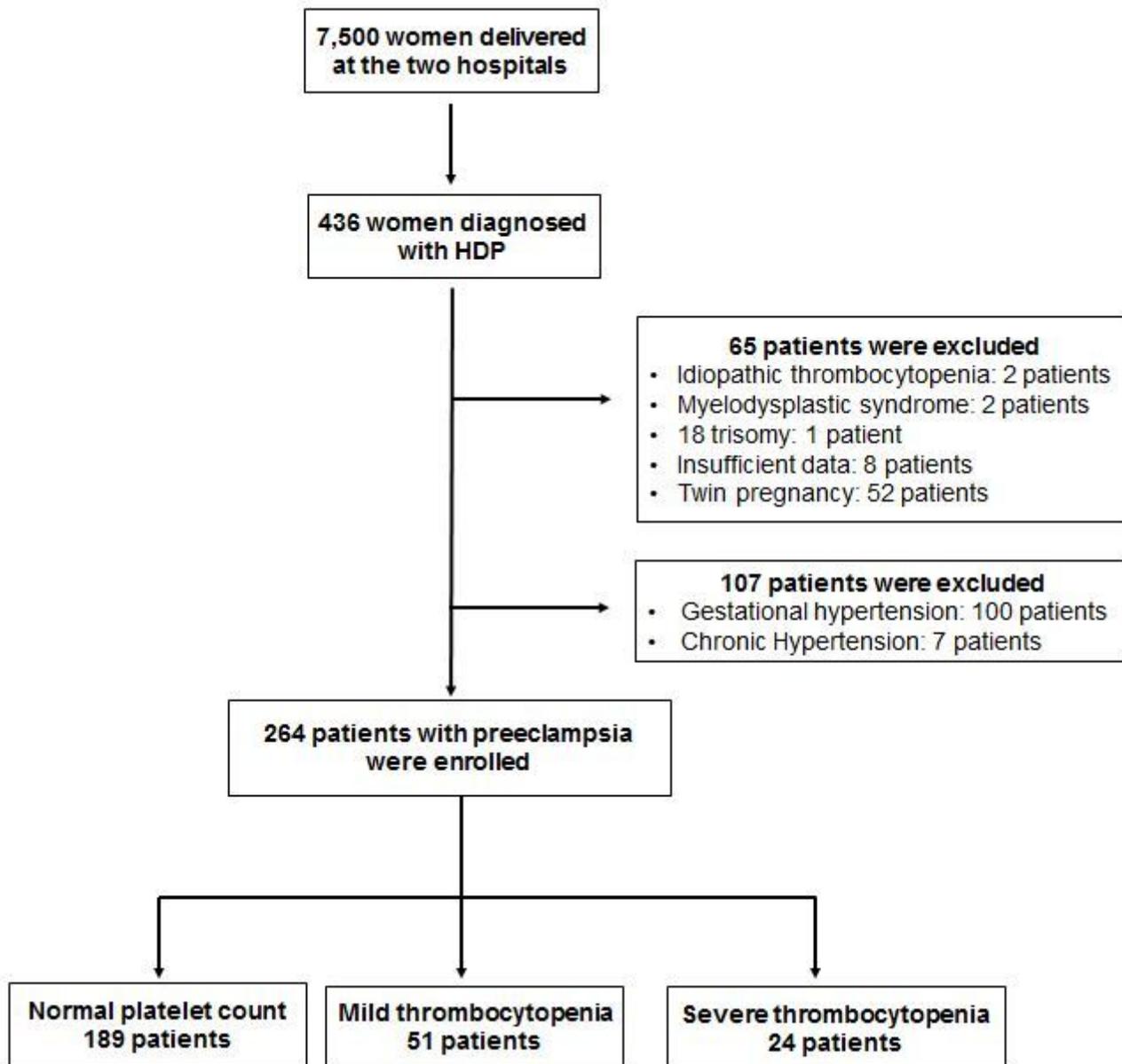


Figure 1

Schematic illustration of the patient selection criteria HDP: hypertensive disorders of pregnancy

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Additionalfile1.docx](#)
- [Additionalfile2.docx](#)
- [Additionalfile3.docx](#)
- [Additionalfile4.docx](#)